10/724,594

```
=> d his

     (FILE 'HOME' ENTERED AT 14:51:02 ON 22 NOV 2004)

     FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS,
     LIFESCI' ENTERED AT 14:51:26 ON 22 NOV 2004
L1       1256226 S KINASE?
L2          1508 S CITRON
L3          2404 S RHO(2W)RAC
L4           226 S L1 AND L2
L5            31 S L3 AND L4
L6            12 DUP REM L5 (19 DUPLICATES REMOVED)
L7       6800229 S CLON? OR EXPRESS? OR RECOMBINANT
L8           112 S L4 AND L7
L9            38 S HUMAN AND L8
L10           25 DUP REM L9 (13 DUPLICATES REMOVED)
                 E WEBSTER M/AU
L11          830 S E3
                 E YAN C/AU
L12         1070 S E3
                 E DIFRANCESCO V/AU
L13          116 S E3-E4
                 E BEASLEY E M/AU
L14          314 S E3
L15         2182 S L11 OR L12 OR L13 OR L14
L16            1 S L4 AND L15
```

```
Connecting via Winsock to STN


Welcome to STN International!  Enter x:x

LOGINID:SSSPTA1652MXM

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2


* * * * * * * * * *   Welcome to STN International   * * * * * * * * * *

 NEWS  1           Web Page URLs for STN Seminar Schedule - N. America
 NEWS  2           "Ask CAS" for self-help around the clock
 NEWS  3  SEP 01   INPADOC: New family current-awareness alert (SDI) available
 NEWS  4  SEP 01   New pricing for the Save Answers for SciFinder Wizard within
                   STN Express with Discover!
 NEWS  5  SEP 01   New display format, HITSTR, available in WPIDS/WPINDEX/WPIX
 NEWS  6  SEP 27   STANDARDS will no longer be available on STN
 NEWS  7  SEP 27   SWETSCAN will no longer be available on STN
 NEWS  8  OCT 28   KOREAPAT now available on STN
 NEWS  9  NOV 18   Current-awareness alerts, saved answer sets, and current
                   search transcripts to be affected by CERAB, COMPUAB, ELCOM,
                   and SOLIDSTATE reloads

 NEWS EXPRESS  OCTOBER 29 CURRENT WINDOWS VERSION IS V7.01A, CURRENT
               MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
               AND CURRENT DISCOVER FILE IS DATED 11 AUGUST 2004
 NEWS HOURS    STN Operating Hours Plus Help Desk Availability
 NEWS INTER    General Internet Information
 NEWS LOGIN    Welcome Banner and News Items
 NEWS PHONE    Direct Dial and Telecommunication Network Access to STN
 NEWS WWW      CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that
specific topic.

  All use of STN is subject to the provisions of the STN Customer
  agreement.  Please note that this agreement limits use to scientific
  research.  Use for software development or design or implementation
  of commercial gateways or other similar uses is prohibited and may
  result in loss of user privileges and other penalties.

  * * * * * * * * * * * * * * STN  Columbus  * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 14:51:02 ON 22 NOV 2004

=> file medline embase biosis biotechds scisearch hcaplus ntis lifesci
COST IN U.S. DOLLARS                        SINCE FILE      TOTAL
                                              ENTRY    SESSION
FULL ESTIMATED COST                            0.21       0.21

FILE 'MEDLINE' ENTERED AT 14:51:26 ON 22 NOV 2004

FILE 'EMBASE' ENTERED AT 14:51:26 ON 22 NOV 2004
COPYRIGHT (C) 2004 Elsevier Inc. All rights reserved.

FILE 'BIOSIS' ENTERED AT 14:51:26 ON 22 NOV 2004
Copyright (c) 2004 The Thomson Corporation.
```

```
FILE 'BIOTECHDS' ENTERED AT 14:51:26 ON 22 NOV 2004
COPYRIGHT (C) 2004 THE THOMSON CORPORATION

FILE 'SCISEARCH' ENTERED AT 14:51:26 ON 22 NOV 2004
Copyright (c) 2004 The Thomson Corporation.

FILE 'HCAPLUS' ENTERED AT 14:51:26 ON 22 NOV 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'NTIS' ENTERED AT 14:51:26 ON 22 NOV 2004
Compiled and distributed by the NTIS, U.S. Department of Commerce.
It contains copyrighted material.
All rights reserved. (2004)

FILE 'LIFESCI' ENTERED AT 14:51:26 ON 22 NOV 2004
COPYRIGHT (C) 2004 Cambridge Scientific Abstracts (CSA)


=> s kinase?
L1     1256226 KINASE?

=> s citron
L2        1508 CITRON

=> s rho(2w)rac
L3        2404 RHO(2W) RAC

=> s l1 and l2
L4         226 L1 AND L2

=> s l3 and l4
L5          31 L3 AND L4

=> dup rem l5
PROCESSING COMPLETED FOR L5
L6           12 DUP REM L5 (19 DUPLICATES REMOVED)

=> d 1-2 ibib ab

L6   ANSWER 1 OF 12  HCAPLUS  COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER:         2004:634054  HCAPLUS
DOCUMENT NUMBER:          141:167789
TITLE:                    Sixty-eight novel genes differentially expressed in
                          tissues relating to urol. disorder and uses thereof in
                          diagnosis, drug screening and treatment of related
                          diseases
INVENTOR(S):              Karicheti, Venkateswarlu; Silos-Santiago, Inmaculada;
                          Eliasof, Scott D.
PATENT ASSIGNEE(S):       Millennium Pharmaceuticals, Inc., USA
SOURCE:                   PCT Int. Appl., 542 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.         DATE
     ---------------      ----   --------    --------------------    --------
     WO 2004065576         A2    20040805    WO 2004-US750           20040114
         W:  AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AZ, AZ, BA, BB, BG,
             BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR,
             CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES,
```

ES, FI, FI, GB, GD, GE, GE, GH, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KP, KR, KR, KZ, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ, MZ, NA, NI

US 2004197825 A1 20041007 US 2004-757262 20040114

PRIORITY APPLN. INFO.: US 2003-440318P P 20030115
US 2003-444783P P 20030204
US 2003-457901P P 20030327
US 2003-468775P P 20030508
US 2003-471614P P 20030519
US 2003-478742P P 20030616
US 2003-488529P P 20030718
US 2003-491156P P 20030730
US 2003-499594P P 20030902
US 2003-506332P P 20030926

AB The present invention relates to methods for the diagnosis and treatment of a urol. disorder or urol. disorders. Specifically, the present invention identifies the differential expression of 68 genes in tissues relating to urol. disorder, relative to their expression in normal, or non-urol. disorder disease states, and/or in response to manipulations relevant to a urol. disorder. Disclosed gene IDs are 44390, 54181, 211, 5687, 884, 1405, 636, 4421, 5410, 30905, 2045, 16405, 18560, 2047, 33751, 52872, 14063, 20739, 32544, 43239, 44373, 51164, 53010, 16852, 1587, 2207, 22245, 2387, 52908, 69112, 14990, 18547, 115, 579, 15985, 15625, 760, 18603, 2395, 2554, 8675, 32720, 4809, 14303, 16816, 17827, 32620, 577, 619, 1423, 2158, 8263, 15402, 16209, 16386, 21165, 30911, 41897, 1643, 2543, 9626, 13231, 32409, 84260, 2882, 8203, 32678 and 55053. Also provided are their cDNA and protein sequences. The present invention describes methods for the diagnostic evaluation and prognosis of various urol. diseases, and for the identification of subjects exhibiting a predisposition to such conditions. The invention also provides methods for identifying a compound capable of modulating a urol. disorder or urol. disorders. The present invention also provides methods for the identification and therapeutic use of compds. as treatments of urol. disorders.

L6 ANSWER 2 OF 12 SCISEARCH COPYRIGHT (c) 2004 The Thomson Corporation. on STN

ACCESSION NUMBER: 2004:855679 SCISEARCH
THE GENUINE ARTICLE: 857AL
TITLE: A new look at Rho GTPases in cell cycle - Role in kinetochore-microtubule attachment
AUTHOR: Narumiya S (Reprint); Oceguera-Yanez F; Yasuda S
CORPORATE SOURCE: Kyoto Univ, Fac Med, Dept Pharmacol, Sakyo Ku, Kyoto 6068501, Japan (Reprint); Kyoto Univ, Fac Med, Horizontal Med Res Org, Kyoto 6068501, Japan
COUNTRY OF AUTHOR: Japan
SOURCE: CELL CYCLE, (JUL 2004) Vol. 3, No. 7, pp. 855-857. Publisher: LANDES BIOSCIENCE, 810 SOUTH CHURCH STREET, GEORGETOWN, TX 78626 USA. ISSN: 1538-4101.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 45

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Rho GTPases including **Rho**, **Rac** and Cdc42 are involved in cell morphogenesis by inducing specific types of actin cytoskeleton and alignment and stabilization of microtubules. Previous studies suggest that they also regulate cell cycle progression; **Rho**, **Rac** and Cdc42 regulate the G(1)-S progression and Rho controls cytokinesis. However, a role of Rho GTPases in nuclear division has not been definitely shown. We have recently found that Cdc42 and its downstream effector mDia3 are involved in bi-orientation and stabilization of spindle microtubules attachment to kinetochores and

regulate chromosome alignment and segregation. Here, we discuss how this is coordinated with other events in mitosis, particularly, with the action of Rho in cytokinesis and how attachment of microtubules to kinetochores is achieved and stabilized. We also discuss redundancy of Cdc42 and Cdc42-related GTPase(s) and potential mechanisms of chromosome instability in cancer.

=> d his

(FILE 'HOME' ENTERED AT 14:51:02 ON 22 NOV 2004)

FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS, LIFESCI' ENTERED AT 14:51:26 ON 22 NOV 2004

```
L1      1256226 S KINASE?
L2         1508 S CITRON
L3         2404 S RHO(2W)RAC
L4          226 S L1 AND L2
L5           31 S L3 AND L4
L6           12 DUP REM L5 (19 DUPLICATES REMOVED)
```

=> d 1-12 ibib ab

L6 ANSWER 1 OF 12 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2004:634054 HCAPLUS
DOCUMENT NUMBER: 141:167789
TITLE: Sixty-eight novel genes differentially expressed in tissues relating to urol. disorder and uses thereof in diagnosis, drug screening and treatment of related diseases
INVENTOR(S): Karicheti, Venkateswarlu; Silos-Santiago, Inmaculada; Eliasof, Scott D.
PATENT ASSIGNEE(S): Millennium Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 542 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2004065576	A2	20040805	WO 2004-US750		20040114
W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KP, KR, KR, KZ, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ, MZ, NA, NI					
US 2004197825	A1	20041007	US 2004-757262		20040114
PRIORITY APPLN. INFO.:			US 2003-440318P	P	20030115
			US 2003-444783P	P	20030204
			US 2003-457901P	P	20030327
			US 2003-468775P	P	20030508
			US 2003-471614P	P	20030519
			US 2003-478742P	P	20030616
			US 2003-488529P	P	20030718
			US 2003-491156P	P	20030730
			US 2003-499594P	P	20030902
			US 2003-506332P	P	20030926

AB The present invention relates to methods for the diagnosis and treatment of a urol. disorder or urol. disorders. Specifically, the present invention identifies the differential expression of 68 genes in tissues

relating to urol. disorder, relative to their expression in normal, or non-urol. disorder disease states, and/or in response to manipulations relevant to a urol. disorder. Disclosed gene IDs are 44390, 54181, 211, 5687, 884, 1405, 636, 4421, 5410, 30905, 2045, 16405, 18560, 2047, 33751, 52872, 14063, 20739, 32544, 43239, 44373, 51164, 53010, 16852, 1587, 2207, 22245, 2387, 52908, 69112, 14990, 18547, 115, 579, 15985, 15625, 760, 18603, 2395, 2554, 8675, 32720, 4809, 14303, 16816, 17827, 32620, 577, 619, 1423, 2158, 8263, 15402, 16209, 16386, 21165, 30911, 41897, 1643, 2543, 9626, 13231, 32409, 84260, 2882, 8203, 32678 and 55053. Also provided are their cDNA and protein sequences. The present invention describes methods for the diagnostic evaluation and prognosis of various urol. diseases, and for the identification of subjects exhibiting a predisposition to such conditions. The invention also provides methods for identifying a compound capable of modulating a urol. disorder or urol. disorders. The present invention also provides methods for the identification and therapeutic use of compds. as treatments of urol. disorders.

L6 ANSWER 2 OF 12 SCISEARCH COPYRIGHT (c) 2004 The Thomson Corporation. on STN

ACCESSION NUMBER: 2004:855679 SCISEARCH
THE GENUINE ARTICLE: 857AL
TITLE: A new look at Rho GTPases in cell cycle - Role in kinetochore-microtubule attachment
AUTHOR: Narumiya S (Reprint); Oceguera-Yanez F; Yasuda S
CORPORATE SOURCE: Kyoto Univ, Fac Med, Dept Pharmacol, Sakyo Ku, Kyoto 6068501, Japan (Reprint); Kyoto Univ, Fac Med, Horizontal Med Res Org, Kyoto 6068501, Japan
COUNTRY OF AUTHOR: Japan
SOURCE: CELL CYCLE, (JUL 2004) Vol. 3, No. 7, pp. 855-857. Publisher: LANDES BIOSCIENCE, 810 SOUTH CHURCH STREET, GEORGETOWN, TX 78626 USA. ISSN: 1538-4101.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 45

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Rho GTPases including **Rho**, **Rac** and Cdc42 are involved in cell morphogenesis by inducing specific types of actin cytoskeleton and alignment and stabilization of microtubules. Previous studies suggest that they also regulate cell cycle progression; **Rho**, **Rac** and Cdc42 regulate the G(1)-S progression and Rho controls cytokinesis. However, a role of Rho GTPases in nuclear division has not been definitely shown. We have recently found that Cdc42 and its downstream effector mDia3 are involved in bi-orientation and stabilization of spindle microtubules attachment to kinetochores and regulate chromosome alignment and segregation. Here, we discuss how this is coordinated with other events in mitosis, particularly, with the action of Rho in cytokinesis and how attachment of microtubules to kinetochores is achieved and stabilized. We also discuss redundancy of Cdc42 and Cdc42-related GTPase(s) and potential mechanisms of chromosome instability in cancer.

L6 ANSWER 3 OF 12 MEDLINE on STN DUPLICATE 1

ACCESSION NUMBER: 2004338572 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15240570
TITLE: Mutations in sticky lead to defective organization of the contractile ring during cytokinesis and are enhanced by Rho and suppressed by Rac.
AUTHOR: D'Avino Pier Paolo; Savoian Matthew S; Glover David M
CORPORATE SOURCE: Cancer Research UK Cell Cycle Genetics Research Group, Department of Genetics, University of Cambridge, Downing Site, CB2 3EH.. p.davino@gen.cam.ac.uk
SOURCE: Journal of cell biology, (2004 Jul 5) 166 (1) 61-71.

Journal code: 0375356. ISSN: 0021-9525.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200408
ENTRY DATE: Entered STN: 20040709
Last Updated on STN: 20040827
Entered Medline: 20040826

AB The contractile ring is a highly dynamic structure, but how this dynamism is accomplished remains unclear. Here, we report the identification and analysis of a novel Drosophila gene, sticky (sti), essential for cytokinesis in all fly proliferating tissues. sti encodes the Drosophila orthologue of the mammalian **Citron kinase**. RNA interference-mediated silencing of sti in cultured cells causes them to become multinucleate. Components of the contractile ring and central spindle are recruited normally in such STICKY-depleted cells that nevertheless display asymmetric furrowing and aberrant blebbing. Together with an unusual distribution of F-actin and Anillin, these phenotypes are consistent with defective organization of the contractile ring. sti shows opposite genetic interactions with **Rho** and **Rac** genes suggesting that these GTPases antagonistically regulate STICKY functions. Similar genetic evidence indicates that RacGAP50C inhibits Rac during cytokinesis. We discuss that antagonism between **Rho** and **Rac** pathways may control contractile ring dynamics during cytokinesis.

L6 ANSWER 4 OF 12 BIOTECHDS COPYRIGHT 2004 THE THOMSON CORP. on STN
DUPLICATE 2
ACCESSION NUMBER: 2003-11097 BIOTECHDS
TITLE: New human **citron rho/rac**-interacting **kinase**-short **kinase** polypeptide and polynucleotide for preventing or treating diseases associated with the polypeptide dysfunction, e.g. obesity or chronic obstructive pulmonary disease; recombinant protein production for use in disease therapy and gene therapy
AUTHOR: ZHU Z
PATENT ASSIGNEE: BAYER AG
PATENT INFO: WO 2003004629 16 Jan 2003
APPLICATION INFO: WO 2002-EP7229 1 Jul 2002
PRIORITY INFO: US 2002-375015 25 Apr 2002; US 2001-301853 2 Jul 2001
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2003-221595 [21]

AB DERWENT ABSTRACT:
NOVELTY - A new isolated polynucleotide (I) which encodes a human **citron rho/rac**-interacting **kinase**-short **kinase** polypeptide (II), is new.
DETAILED DESCRIPTION - A new isolated polynucleotide (I) selected from a polynucleotide: (a) which encodes a human **citron rho/rac**-interacting **kinase**-short **kinase** polypeptide (II) (which comprises a sequence of 495 (S3) or 497 (S4) amino acids fully defined in the specification, or a sequence that is at least 88% identical to S3 or S4); (b) which comprises a sequence of 1485 (S1) or 1765 (S2) bp given in the specification; (c) which hybridizes under stringent conditions to the polynucleotide in (a) and (b); (d) which has a sequence deviating from (a)-(c) due to the degeneration of the genetic code; and (e) which represents a fragment, derivative or allelic variation of (a)-(d). INDEPENDENT CLAIMS are also included for the following: (1) an expression vector containing the above polynucleotide; (2) a host cell comprising the expression vector; (3) a substantially purified human **citron rho/rac**-interacting **kinase**-short **kinase** polypeptide encoded

by (I); (4) producing (II); (5) detecting the above polynucleotide or polypeptide; (6) a diagnostic kit for conducting method (5); (7) screening for agents which regulate or decrease the activity of the **citron rho/rac**-interacting **kinase** -short **kinase** polypeptide; (8) reducing the activity of human **citron rho/rac**-interacting **kinase** -short **kinase** polypeptide; (9) a reagent that modulates the activity of (II) or the polynucleotide cited above, which is identified by method (7); and (10) a pharmaceutical composition comprising the above expression vector or reagent, and a carrier.

BIOTECHNOLOGY - Preferred Method: Producing a human **citron rho/rac**-interacting **kinase**-short **kinase** polypeptide comprises culturing the host cell under conditions suitable for the expression of (II), and recovering the polypeptide from the host cell culture. Detecting the polynucleotide encoding the human **citron rho/rac** -interacting **kinase**-short **kinase** polypeptide in a biological sample, comprises hybridizing the above polynucleotide to a nucleic acid material of a biological sample to form a hybridization complex, and detecting the complex formed. Before hybridization, the nucleic acid material of the biological sample is amplified. Detecting the above polynucleotide or polypeptide comprises contacting a biological sample with a reagent which specifically interacts with the polynucleotide or the polypeptide, and detecting the interaction. Screening for agents which decrease the activity of a human **citron rho/rac**-interacting **kinase** -short **kinase** polypeptide, comprises contacting a test compound with the above polypeptide or polynucleotide, and detecting the binding of the test compound to (II) or the polynucleotide, where a test compound which binds to the polypeptide or the polynucleotide is identified as a potential therapeutic agent for decreasing the activity of the human **citron rho/rac**-interacting **kinase** -short **kinase** polypeptide. In screening for agents which regulate the activity of the above polypeptide, the test compound is contacted with (II), and the activity of the human **citron rho/rac**-interacting **kinase**-short **kinase** polypeptide is detected, where the test compound which increases or decreases the **kinase** activity is identified as a potential therapeutic agent for increasing or decreasing the activity of the **kinase**. Reducing the activity of the human **citron rho/rac**-interacting **kinase**-short **kinase** comprises contacting a cell with a reagent which specifically binds to the above polypeptide or polynucleotide, where the activity of the **kinase** is reduced.

ACTIVITY - Anorectic; Antiinflammatory; Hypotensive; Antidiabetic; Cardiant; Antilipemic; Cerebroprotective; Antigout; Osteopathic; Antiarthritic; Cytostatic; Thrombolytic; Anticoagulant; Gynecological; Antidepressant. No biological data is given.

MECHANISM OF ACTION - Gene therapy.

USE - The polynucleotide and polypeptide are useful in preventing, ameliorating, or treating diseases associated with the polypeptide dysfunction. The expression vector or the reagent is useful in the preparation of a medicament for modulating the activity of a human **citron rho/rac**-interacting **kinase** -short **kinase** in a disease, such as obesity or chronic obstructive pulmonary disease (claimed). These may also be used for treating obesity/overweight-associated comorbidities, such as hypertension, diabetes, coronary artery disease, hyperlipidemia, stroke, gallbladder disease, gout, osteoarthritis, sleep apnea, cancer, thrombolic diseases, polycystic ovarian syndrome, reduced fertility, and depression. The polypeptide and polynucleotide are also useful in diagnostic assays or in genetic testing.

ADMINISTRATION - The dosage ranges from 0.1-100000 microg, up to a total dose of 1 g, depending upon the route of administration, which may

be oral, parenteral (e.g. intravenous, intramuscular, intraarterial, subcutaneous), intramedullary, intrathecal, intraventricular, transdermal, intraperitoneal, intranasal, topical, sublingual, or rectal means.

EXAMPLE - No relevant example given. (73 pages)

L6 ANSWER 5 OF 12 BIOTECHDS COPYRIGHT 2004 THE THOMSON CORP. on STN
DUPLICATE 3

ACCESSION NUMBER: 2003-11086 BIOTECHDS
TITLE: New human **citron rho/rac** -interacting **kinase** (CRIK) polypeptide and polynucleotide, useful in preventing, ameliorating or treating diseases associated with human CRIK dysfunction, e.g. obesity, diabetes or Alzheimer's disease; vector-mediated gene transfer and expression in host cell for recombinant protein production, drug screening and gene therapy
AUTHOR: ZHU Z
PATENT ASSIGNEE: BAYER AG
PATENT INFO: WO 2003004523 16 Jan 2003
APPLICATION INFO: WO 2002-EP7156 28 Jun 2002
PRIORITY INFO: US 2002-375014 25 Apr 2002; US 2001-301841 2 Jul 2001
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2003-221576 [21]

AB DERWENT ABSTRACT:

NOVELTY - An isolated polynucleotide (I) encoding a human **citron rho/rac**-interacting **kinase** polypeptide, comprising a 6165 or 8603 base pair sequence (S1), given in the specification, hybridizing under stringent conditions to them, deviating from them due to the degeneration of the genetic code, or a fragment, derivative or allelic variation of them, is new.

DETAILED DESCRIPTION - An isolated polynucleotide (I) encoding a human **citron rho/rac**-interacting **kinase** polypeptide, comprising a 6165 or 8603 base pair sequence (S1), given in the specification, hybridizing under stringent conditions to them, deviating from them due to the degeneration of the genetic code, or a fragment, derivative or allelic variation of them, is new. (I) encodes a 2054 residue amino acid sequence (S2), given in the specification, or amino acid sequences that are at least 97 % identical to the sequence of S2. INDEPENDENT CLAIMS are included for the following: (1) a substantially purified human CRIK polypeptide encoded by (I); (2) an expression vector containing (I); (3) a host cell containing the expression vector of (2); (4) producing a human CRIK polypeptide; (5) detecting a polynucleotide encoding a human CRIK polypeptide in a biological sample; (6) detecting (I) or a human CRIK polypeptide; (7) a diagnostic kit for conducting the method of (5) or (6); (8) screening for agents that regulate or decrease the activity of a human CRIK; (9) reducing the activity of human CRIK; (10) a reagent that modulates the activity of a human CRIK polypeptide or polynucleotide, where the reagent is identified by the method of (8); and (11) a pharmaceutical composition comprising the expression vector or the reagent, and a pharmaceutical carrier.

BIOTECHNOLOGY - Preparation: The polynucleotide can be made by a cell and isolated using standard nucleic acid purification techniques, or synthesized using an amplification technique, such as PCR, or by using an automatic synthesizer. Preferred Method: Producing a human **citron rho/rac**-interacting **kinase** (CRIK) polypeptide comprises culturing the host cell under conditions suitable for the expression of the polypeptide, and recovering the polypeptide from the host cell culture. Detecting a polynucleotide encoding a human CRIK polypeptide in a biological sample comprises hybridizing (I) to a nucleic acid material of a biological sample to form a hybridization complex, and detecting the hybridization complex formed. Before hybridization, the

nucleic acid material of the biological sample is amplified. Detecting (I) or a human CRIK polypeptide comprises contacting a biological sample with a reagent that specifically interacts with the polynucleotide or the polypeptide, and detecting the interaction. Screening for agents that decrease the activity of a human CRIK comprises contacting a test compound with a human CRIK polypeptide encoded by (I), or with (I), and detecting binding of the test compound to the polypeptide or (I), where a test compound that binds to the polypeptide or polynucleotide is identified as a potential therapeutic agent for decreasing the activity of a human CRIK. Screening for agents that regulate the activity of a human CRIK comprises contacting a test compound with a human CRIK polypeptide encoded by (I), and detecting a human CRIK activity of the polypeptide, where a test compound that increases or decreases the human CRIK activity is identified as a potential therapeutic agent for increasing or decreasing, respectively, the activity of the human CRIK. Reducing the activity of human CRIK comprises contacting a cell with a reagent that specifically binds to human CRIK polypeptide or (I), where the activity of human CRIK is reduced.

ACTIVITY - Anorectic; Hypotensive; Cardiant; Antilipemic; Cerebroprotective; Antigout; Osteopathic; Antiarthritic; Cytostatic; Antidepressant; Immunomodulator; Antimanic; Tranquilizer; Antiparkinsonian; Nootropic; Neuroprotective; Antiinflammatory; Antidiabetic; Analgesic. No biological data is given.

MECHANISM OF ACTION - **Kinase** Inhibitor; **Kinase** Stimulator; Gene Therapy.

USE - The human **citron rho/rac** -interacting **kinase** (CRIK) polypeptide and polynucleotide are useful in preventing, ameliorating, or treating diseases associated with human CRIK dysfunction such as obesity and obesity-associated comorbidities (e.g. hypertension, coronary artery disease, hyperlipidemia, stroke, gout, osteoarthritis, some types of cancer including endometrial, breast, prostate and colon cancer), anorexia, cachexia, bulimia, central nervous system disorders (e.g. mood disorders, anxiety disorders, Parkinson's disease or Alzheimer's disease), chronic obstructive pulmonary disease, or diabetes. These can also be used to treat pain associated with the disorders. The human CRIK polypeptide is also useful in diagnostic assays or in genetic testing. The expression vector or the reagent is useful in preparing a medicament for modulating the activity of a human CRIK in a disease, e.g. obesity, a central nervous system disorder, or chronic obstructive pulmonary disease. (All claimed.) The fusion protein is useful for generating antibodies against CRIK polypeptide and for use in various assay systems. The methods are useful in producing and detecting the polynucleotide and polypeptide and in screening for agents that modulate the activity of the human CRIK polypeptide.

ADMINISTRATION - The dosage ranges from 0.1-100000 micro-g, up to a total dose of about 1g. Administration may be oral, intravenous, intramuscular, intra-arterial, subcutaneous, intramedullary, intrathecal, intraventricular, transdermal, intraperitoneal, intranasal, topical, sublingual, or rectal means.

EXAMPLE - No relevant example given.(237 pages)

L6 ANSWER 6 OF 12 BIOTECHDS COPYRIGHT 2004 THE THOMSON CORP. on STN
ACCESSION NUMBER: 2002-18283 BIOTECHDS
TITLE: Novel isolated NOVX polypeptides and polynucleotides homologous to attractin, plexin, papin-like family of proteins, useful for treating atherosclerosis, diabetes, cancer, Alzheimer's disease, hemophilia and stroke; recombinant protein production and sense and antisense sequence use in disease therapy and gene therapy
AUTHOR: GERLACH V L; MACDOUGALL J R; SMITHSON G; MILLET I; STONE D; GUNTHER E; ELLERMAN K; GROSSE W M; ALSOBROOK J P; LEPLEY D M; BURGESS C E; PADIGARU M; KEKUDA R; SPYTEK K A; LEACH M D; SHIMKETS R A

PATENT ASSIGNEE: CURAGEN CORP
PATENT INFO: WO 2002026826 4 Apr 2002
APPLICATION INFO: WO 2000-US42336 27 Sep 2000
PRIORITY INFO: US 2001-235631 26 Sep 2001
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2002-499860 [53]

AB DERWENT ABSTRACT:

NOVELTY - An isolated NOVX polypeptide (I) comprising an amino acid sequence of mature form of sequence or amino sequence (S) of 841, 837, 1185, 2066, 2053, 1896, 480, 879, 442, 2814 or 2811 amino acids fully defined in specification or a variant of the above that differs not more than 15% of amino acid residues, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following: (1) an isolated nucleic acid molecule (II) comprising a nucleic acid sequence encoding (I); a nucleic acid fragment encoding a portion of a polypeptide comprising (S1) or its variant that differs not more than 15% of amino acid residues and a nucleic acid molecule comprising the complement of the above; (2) a vector (III) comprising (II); (3) an antibody (IV) that binds specifically to (I); (4) a cell (V) comprising (III); (5) modulating the activity of (I) comprising contacting a cell sample expressing (I) with a compound that binds to (I); (6) a pharmaceutical composition (VI) comprising (I), (II) or (IV); and (7) a kit comprising (VI), in one or more containers.

WIDER DISCLOSURE - The following are also disclosed: (1) immunoconjugates comprising (IV) conjugated to a cytotoxic agent;(2) derivatives, analogs and homologs of (II); (3) NOVX chimeric or fusion proteins, useful therapeutically, in purification of NOVX ligands, producing anti-NOVX antibodies, and in screening assays; (4) isolated antisense nucleic acids that are hybridizable or complementary to (II); and (5) a kit for detecting presence of NOVX in a sample.

BIOTECHNOLOGY - Preparation: (I) is produced by recombinant DNA techniques. Preferred Polypeptide: In (I), the amino acid sequence of the variant comprises a conservative amino acid substitution. (I) comprises the amino acid sequence of a naturally occurring allelic variant of (S1) i.e. the translation of a nucleic acid sequence differing by a single nucleotide from a nucleic acid sequence (S2) of 2838, 2526, 2531, 3609, 6201, 6189, 5691, 1535, 2657, 1366, 1421, 2024, 8640 or 8640 nucleotides fully defined in the specification. NOV1 is homologous to a insulin like growth factor binding protein complex-acid labile subunit-like family of proteins, NOV2 is homologous to attractin-like family of proteins, and NOV3 is homologous to a family of **RHO/RAC**-interacting **citron kinase**-like proteins. NOV4 is homologous to the plexin-like family of proteins, NOV5 is homologous to the dopamine receptor-like family of proteins, and NOV6 is homologous to the metabotropic glutamate receptor-like family of proteins. NOV7 is homologous to members of PV-like family of proteins, and NOV8 is homologous to papin-like family of proteins. Preferred Nucleic Acid: (II) comprises the nucleotide sequence of a naturally occurring allelic nucleic acid variant, and encodes a polypeptide comprising the amino acid sequence of a naturally occurring polypeptide variant. (II) comprises a nucleotide sequence of (S2) or a sequence differing by one or more nucleotides from (S2) but does not differ more than 20% of the nucleotides and a nucleic acid fragment of the above. (II) hybridizes to (S2) or to its complement. In (II), the nucleic acid molecule comprises a sequence of a first nucleotide sequence comprising a coding sequence differing by one or more nucleotide sequences from a coding sequence encoding the amino acid sequence, provided that not more than 20% of the nucleotides in the coding sequence in the first nucleotide sequence differ from the coding sequence; an isolated second polynucleotide complementary to the first polynucleotide; and a nucleic acid fragment of the above. Preferred Vector: (III) further comprising a promoter operably-linked to the nucleic acid molecule.

ACTIVITY - Cytostatic; Uropathic, Gynecological; Hepatotropic;

Antiinflammatory; Antiinfertility; Antilipemic; Antiarteriosclerotic; Hypotensive; Dermatological; Hemostatic; Anorectic; Antidiabetic; Immunosuppressive; Antiasthmatic; Antipsoriatic; Antiallergic; Nootropic; Neuroprotective; Cerebroprotective; Antiparkinsonian; Anticonvulsant; Tranquilizer; Analgesic; Neuroleptic; Antialcoholic; Nephrotropic. No supporting data given.

MECHANISM OF ACTION - Modulator of expression of NOVX polypeptide; Gene therapy; Vaccine. No supporting data given.

USE - (I), (II) or (IV) is useful in treating or preventing a NOVX-associated disorder which is cardiomyopathy, atherosclerosis and diabetes in a human, where the disorder is related to cell signal processing and metabolic pathway modulation. (IV) is useful for determining the presence or amount of (I) in a sample. Fragment of (I) is useful as probe for determining the presence or amount of (II) in the sample. The presence or amount of (II) is useful as a marker for cancerous cell or tissue type. (I) is useful for identifying an agent which is cellular receptor or downstream effector. (I) is also useful for identifying an agent that modulates the expression or activity of (I). (I) or (II) is useful for determining the presence or predisposition to a disease associated with altered levels of (I) or (II), especially cancer. Polypeptide 95% identical to (I) or its biologically active fragment, or (IV) is useful for treating a pathological state in a mammal (claimed). (I) is useful as immunogen to produce (IV), and as vaccines and is also useful in screening for potential agonist and antagonist compounds. (I) is useful for screening for a modulator of activity or of latency or predisposition to disorders. Fragments of (I) (cDNA) sequence useful in chromosome mapping, tissue typing and in forensic identification of a biological sample. Probes obtained from (II) is useful for detecting transcripts or genomic sequences encoding the same or homologous proteins and identifying cells or tissues that misexpress an NOVX protein. (II) is useful in gene therapy, and in purification of (I). (II) is useful to express NOVX protein, to detect NOVX mRNA or a genetic lesion in an NOVX gene and to modulate NOVX activity. (I) or (II) is useful for prognostic (predictive) assays, for prophylactically treating an individual. Agent that modulate NOVX expression is useful for preventing or treating diseases. (I), (II) or (III) is useful in treating diseases such as hypertension, congenital heart defects, aortic stenosis, obesity, infectious disease, anorexia, cancer, Alzheimer's disease, Parkinson's disorders, neurodegenerative disorders, hemophilia, dyslipidemias, hematopoietic diseases, scleroderma, fertility, idiopathic thrombocytopenic purpura, graft versus host diseases, Crohn's disease, multiple sclerosis, cirrhosis, autoimmune disease, systemic lupus erythematosus, asthma, arthritis, psoriasis, allergy, stroke, anxiety, Lesch-Nyhan syndrome, schizophrenia, cerebellar ataxia, pain and alcoholism. (IV) is useful to detect and isolate NOVX proteins and modulate NOVX activity. (V) is useful to produce non-human transgenic animals which is useful for studying the function and/or activity of NOVX protein and for identifying and/or evaluating modulators of NOVX protein activity.

ADMINISTRATION - Administered by parenteral, oral, transdermal, transmucosal or rectal route. No dosage is given.

EXAMPLE - The polymerase chain reaction (PCR) primers used were primer 1: (5'-3') NOVIC: TCATCACATGACAACATGAAGCTGT and NOV7a: CCAATCTCTGATGCCCTGCGAT, primer 2 (5'-3') NOVIC: GAAAGCCCTCAAACTCTCCATCTATG and NOV7a: AGGTCAGTGCCGGAGCCTCC. These primers were designed based on silico predictions for the full length cDNA, part (one or more exons) of the DNA or protein sequence of the target sequence or by translated homology of the predicted exons to closely related human sequences from other species. These primers were then employed in PCR amplification based on the pool of human cDNAs like adrenal gland, bone marrow, brain-whole fetal brain, pancreas, pituitary gland, placenta, prostate, salivary gland, skeletal muscle, small intestine, spinal cord, spleen, stomach, testis, thyroid, trachea and uterus. The resulting amplicons were gel purified, cloned and sequenced to high redundancy. The

PCR product derived from exon linking was cloned into the PCR2.1 vector. The resulting bacterial clone had an insert covering the entire open reading frame cloned into the PCR2.1 vector. The resulting sequences from all clones were assembled with themselves, with other fragments in CuraGen Corporations database and with public expressed sequence tags (ESTs). Fragment and ESTs were included as components for an assembly when the extent of the identity with another component of the assembly was 95% over 50 bp. Sequence traces were evaluated manually and edited for corrections. Thus, the sequences encoding the full length NOVX protein of 841, 837, 1185, 2066, 2053, 1896, 480, 879, 442, 2814 or 2811 amino acids defined in the specification, was obtained. (308 pages)

L6 ANSWER 7 OF 12 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:716956 HCAPLUS
DOCUMENT NUMBER: 137:259346
TITLE: Identification, cloning, genomic and cDNA sequences and use of human **citron kinase** family member
INVENTOR(S): Webster, Marion; Yan, Chunhua; Di Francesco, Valentina; Beasley, Ellen M.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 184 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002132322	A1	20020919	US 2001-804471	20010313
US 6479269	B2	20021112		
US 6638745	B1	20031028	US 2001-916204	20010727
US 2003022340	A1	20030130	US 2002-238709	20020911
US 6680188	B2	20040120		
US 2003049795	A1	20030313	US 2002-282048	20021029
US 6692948	B2	20040217		
US 2004091993	A1	20040513	US 2003-724594	20031202

PRIORITY APPLN. INFO.: US 2001-804471 A2 20010313
US 2001-916204 A3 20010727
US 2002-238709 A3 20020911

AB The present invention provides amino acid sequences of peptides that are encoded by genes within the human genome, the **kinase** peptides of the present invention. The cDNA sequence and the encoded amino acid sequence of the human **kinase** that is related to the **rho**/**rac**-interacting **citron kinase** (CRIK) subfamily are provided. Chromosomal mapping of the **citron kinase** gene, tissue-specific expression profiles, and structural motifs of the polypeptide are provided. The genomic sequence of the **citron kinase** gene and SNPs that have been found in the gene are disclosed. The present invention specifically provides isolated peptide and nucleic acid mols., methods of identifying orthologs and paralogs of the **citron kinase** peptides, and methods of identifying modulators of the **citron kinase** peptides.

L6 ANSWER 8 OF 12 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:281034 HCAPLUS
DOCUMENT NUMBER: 130:307992
TITLE: Effectors of Rho family of GTPases. Recent progress
AUTHOR(S): Watanabe, Naoki; Ishizaki, Toshimasa
CORPORATE SOURCE: Fac. Med., Kyoto Univ., Japan
SOURCE: Jikken Igaku (1999), 17(7), 824-830
CODEN: JIIGEF; ISSN: 0288-5514
PUBLISHER: Yodosha

DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese
AB A review with 25 refs., on properties and functions of Rho effectors (ROCK/Rho **kinase**, **Citron**-K/**Citron**-N, Rhophilin, p140mDia/mDia2, ACK, WASP/N-WASP, etc.) involved in regulation of actin cytoskeleton by Rho family, including **Rho**, **Rac**, and Cdc42. Roles of Rho effectors in cytokinesis and localization of Rhophilin in the tail of spermatid are also discussed.

L6 ANSWER 9 OF 12 MEDLINE on STN DUPLICATE 4
ACCESSION NUMBER: 1999009084 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9792683
TITLE: **Citron** rho-interacting **kinase**, a novel tissue-specific ser/thr **kinase** encompassing the **Rho-Rac**-binding protein **Citron**.
AUTHOR: Di Cunto F; Calautti E; Hsiao J; Ong L; Topley G; Turco E; Dotto G P
CORPORATE SOURCE: Cutaneous Biology Research Center, Massachusetts General Hospital and Harvard Medical School, Charlestown, Massachusetts 02129, USA.
CONTRACT NUMBER: AR39190 (NIAMS)
CA16038 (NCI)
CA73796 (NCI)
SOURCE: Journal of biological chemistry, (1998 Nov 6) 273 (45) 29706-11.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AF086823; GENBANK-AF086824
ENTRY MONTH: 199812
ENTRY DATE: Entered STN: 19990115
Last Updated on STN: 20020420
Entered Medline: 19981210
AB We have identified a novel serine/threonine **kinase** belonging to the myotonic dystrophy **kinase** family. The **kinase** can be produced in at least two different isoforms: a approximately 240-kDa protein (**Citron** Rho-interacting **kinase**, CRIK), in which the **kinase** domain is followed by the sequence of **Citron**, a previously identified **Rho/Rac** binding protein; a approximately 54-kDa protein (CRIK-short **kinase** (SK)), which consists mostly of the **kinase** domain. CRIK and CRIK-SK proteins are capable of phosphorylating exogenous substrates as well as of autophosphorylation, when tested by in vitro **kinase** assays after expression into COS7 cells. CRIK **kinase** activity is increased severalfold by coexpression of costitutively active **Rho**, while active **Rac** has more limited effects. **Kinase** activity of endogenous CRIK is indicated by in vitro **kinase** assays after immunoprecipitation with antibodies recognizing the **Citron** moiety of the protein. When expressed in keratinocytes, full-length CRIK, but not CRIK-SK, localizes into corpuscular cytoplasmic structures and elicits recruitment of actin into these structures. The previously reported Rho-associated **kinases** ROCK I and II are ubiquitously expressed. In contrast, CRIK exhibits a restricted pattern of expression, suggesting that this **kinase** may fulfill a more specialized function in specific cell types.

L6 ANSWER 10 OF 12 MEDLINE on STN DUPLICATE 5
ACCESSION NUMBER: 1998334623 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9668072
TITLE: Different regions of Rho determine Rho-selective binding of different classes of Rho target molecules.
AUTHOR: Fujisawa K; Madaule P; Ishizaki T; Watanabe G; Bito H;

Saito Y; Hall A; Narumiya S
CORPORATE SOURCE: Department of Pharmacology, Kyoto University Faculty of Medicine, Sakyo-ku, Kyoto 606, Japan.
SOURCE: Journal of biological chemistry, (1998 Jul 24) 273 (30) 18943-9.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199808
ENTRY DATE: Entered STN: 19980828
Last Updated on STN: 20020420
Entered Medline: 19980820

AB Based on their Rho binding motifs several Rho target molecules can be classified into three groups; class I includes the protein **kinase** PKN, rhophilin, and rhotekin, class II includes the protein **kinases**, Rho-associated coiled-coil containing protein **kinases**, ROCK-I and ROCK-II, and class III includes **citron** . Taking advantage of the selectivity in recognition by these targets between **Rho** and **Rac**, we examined the regions in Rho required for selective binding of each class of Rho target molecules. Yeast two-hybrid assays were performed using **Rho/Rac** chimeras and either rhophilin, ROCK-I, or **citron**. This study showed the existence of at least two distinct regions in Rho (amino acids 23-40 and 75-92) that are critical for the selective binding of these targets. The former was required for binding to **citron**, whereas the latter was necessary for binding to rhophilin. On the other hand, either region showed affinity to ROCK-I. This was further confirmed by ligand overlay assay using both recombinant ROCK-I and ROCK-II proteins. Consistently, **Rho/Rac** chimeras containing either region can induce stress fibers in transfected HeLa cells, and this induction is suppressed by treatment with Y-27632, a specific inhibitor of ROCK **kinases**. These results suggest that the selective binding of different classes of Rho targets to Rho is determined by interaction between distinct Rho-binding motifs of the targets and different regions of Rho.

L6 ANSWER 11 OF 12 MEDLINE on STN DUPLICATE 6
ACCESSION NUMBER: 1998316249 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9651538
TITLE: Signal transduction molecules at the glutamatergic postsynaptic membrane.
AUTHOR: Kennedy M B
CORPORATE SOURCE: Division of Biology 216-76, California Institute of Technology, Pasadena, CA 91125, USA..
kennedym@cco.caltech.edu
CONTRACT NUMBER: GMS07616 (NIGMS)
NS17660 (NINDS)
NS28710 (NINDS)
+
SOURCE: Brain research. Brain research reviews, (1998 May) 26 (2-3) 243-57. Ref: 108
Journal code: 8908638. ISSN: 0165-0173.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199808
ENTRY DATE: Entered STN: 19980910
Last Updated on STN: 20000303
Entered Medline: 19980828

AB We have applied techniques from modern molecular biology and biochemistry to unravel the complex molecular structure of the postsynaptic membrane at glutamatergic synapses in the central nervous system. We have characterized a set of new proteins that are constituents of the postsynaptic density, including PSD-95, densin-180, **citron** (a **rho/rac** effector protein), and synaptic gp130 Ras GAP (a new Ras GTPase-activating protein). The structure of PSD-95 revealed a new protein motif, the PDZ domain, that plays an important role in the assembly of signal transduction complexes at intercellular junctions. More recently, we have used new imaging tools to observe the dynamics of autophosphorylation of CaM **kinase** II in intact hippocampal tissue. We have been able to detect changes in the amount of autophosphorylated CaM **kinase** II in dendrites, individual synapses, and somas of hippocampal neurons following induction of long-term potentiation by tetanic stimulation. In addition, we have observed a specific increase in the concentration of CaM **kinase** II in dendrites of neurons receiving tetanic stimulation. This increase appears to be the result of dendritic synthesis of new protein. Over the next several years we will apply similar methods to study regulatory changes that occur at the molecular level in glutamatergic synapses in the CNS as the brain processes and stores new information.

L6 ANSWER 12 OF 12 SCISEARCH COPYRIGHT (c) 2004 The Thomson Corporation. on STN
ACCESSION NUMBER: 96:48446 SCISEARCH
THE GENUINE ARTICLE: TM328
TITLE: A NOVEL PARTNER FOR THE GTP-BOUND FORMS OF **RHO** AND **RAC**
AUTHOR: MADAULE P; FURUYASHIKI T; REID T; ISHIZAKI T; WATANABE G; MORII N; NARUMIYA S (Reprint)
CORPORATE SOURCE: KYOTO UNIV, FAC MED, DEPT PHARMACOL 2, SAKYO KU, KYOTO 606, JAPAN (Reprint); KYOTO UNIV, FAC MED, DEPT PHARMACOL 2, SAKYO KU, KYOTO 606, JAPAN
COUNTRY OF AUTHOR: JAPAN
SOURCE: FEBS LETTERS, (18 DEC 1995) Vol. 377, No. 2, pp. 243-248. ISSN: 0014-5793.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: ENGLISH
REFERENCE COUNT: 26
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB Using the yeast two hybrid system and overlay assays me identified a putative rholrac effector, **citron**, which interacts with the GTP-bound forms of rho and rac1, but not with cdc42. Extensive homologies to known proteins were not observed. This 183 kDa protein contains a C6H2 zinc finger, a PH domain, and a long coiled-coil forming region including 4 leucine zippers and the rholrac binding site, We recently identified three others putative rho effecters characterized by a common rho binding motif. **Citron** does not share this motif and displays a distinctive protein organization, thus defining a separate class of rho partners.

=> d his

(FILE 'HOME' ENTERED AT 14:51:02 ON 22 NOV 2004)

FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS, LIFESCI' ENTERED AT 14:51:26 ON 22 NOV 2004
L1 1256226 S KINASE?
L2 1508 S CITRON
L3 2404 S RHO(2W)RAC
L4 226 S L1 AND L2

```
L5            31 S L3 AND L4
L6            12 DUP REM L5 (19 DUPLICATES REMOVED)

=> s clon? or express? or recombinant
   4 FILES SEARCHED...
L7      6800229 CLON? OR EXPRESS? OR RECOMBINANT

=> s l4 and l7
L8          112 L4 AND L7

=> s human and l8
L9           38 HUMAN AND L8

=> dup rem l9
PROCESSING COMPLETED FOR L9
L10          25 DUP REM L9 (13 DUPLICATES REMOVED)

=> d 1-25 ibib ab

L10  ANSWER 1 OF 25  HCAPLUS  COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER:         2004:634054  HCAPLUS
DOCUMENT NUMBER:          141:167789
TITLE:                    Sixty-eight novel genes differentially
                          expressed in tissues relating to urol.
                          disorder and uses thereof in diagnosis, drug screening
                          and treatment of related diseases
INVENTOR(S):              Karicheti, Venkateswarlu; Silos-Santiago, Inmaculada;
                          Eliasof, Scott D.
PATENT ASSIGNEE(S):       Millennium Pharmaceuticals, Inc., USA
SOURCE:                   PCT Int. Appl., 542 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.          DATE
     ---------------      ----   --------    --------------------     --------
     WO 2004065576         A2    20040805    WO 2004-US750            20040114
         W:  AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AZ, AZ, BA, BB, BG,
             BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR,
             CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES,
             ES, FI, FI, GB, GD, GE, GE, GH, GM, HR, HR, HU, HU, ID, IL, IN,
             IS, JP, JP, KE, KE, KG, KG, KP, KP, KP, KR, KR, KZ, KZ, KZ, LC,
             LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX,
             MZ, MZ, NA, NI
     US 2004197825         A1    20041007    US 2004-757262           20040114
PRIORITY APPLN. INFO.:                     US 2003-440318P     P  20030115
                                           US 2003-444783P     P  20030204
                                           US 2003-457901P     P  20030327
                                           US 2003-468775P     P  20030508
                                           US 2003-471614P     P  20030519
                                           US 2003-478742P     P  20030616
                                           US 2003-488529P     P  20030718
                                           US 2003-491156P     P  20030730
                                           US 2003-499594P     P  20030902
                                           US 2003-506332P     P  20030926
AB   The present invention relates to methods for the diagnosis and treatment
     of a urol. disorder or urol. disorders.  Specifically, the present
     invention identifies the differential expression of 68 genes in
     tissues relating to urol. disorder, relative to their expression
     in normal, or non-urol. disorder disease states, and/or in response to
     manipulations relevant to a urol. disorder.  Disclosed gene IDs are 44390,
     54181, 211, 5687, 884, 1405, 636, 4421, 5410, 30905, 2045, 16405, 18560,
```

2047, 33751, 52872, 14063, 20739, 32544, 43239, 44373, 51164, 53010, 16852, 1587, 2207, 22245, 2387, 52908, 69112, 14990, 18547, 115, 579, 15985, 15625, 760, 18603, 2395, 2554, 8675, 32720, 4809, 14303, 16816, 17827, 32620, 577, 619, 1423, 2158, 8263, 15402, 16209, 16386, 21165, 30911, 41897, 1643, 2543, 9626, 13231, 32409, 84260, 2882, 8203, 32678 and 55053. Also provided are their cDNA and protein sequences. The present invention describes methods for the diagnostic evaluation and prognosis of various urol. diseases, and for the identification of subjects exhibiting a predisposition to such conditions. The invention also provides methods for identifying a compound capable of modulating a urol. disorder or urol. disorders. The present invention also provides methods for the identification and therapeutic use of compds. as treatments of urol. disorders.

L10 ANSWER 2 OF 25 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:219931 HCAPLUS
DOCUMENT NUMBER: 140:248186
TITLE: Use of patterns of gene **expression** to identify tissue types and in disease diagnosis and prognosis
INVENTOR(S): Glinskii, Guennadi V.
PATENT ASSIGNEE(S): Sidney Kimmel Cancer Center, USA
SOURCE: U.S. Pat. Appl. Publ., 209 pp., which which which which
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004053317	A1	20040318	US 2003-660434	20030910
WO 2004025258	A2	20040325	WO 2003-US28707	20030910

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:

US 2002-410018P	P	20020910
US 2002-411155P	P	20020916
US 2002-429168P	P	20021125
US 2003-444348P	P	20030131
US 2003-460826P	P	20030403

AB Methods of using quant. anal. of array hybridizations to identify normal and diseased tissue in the diagnosis and prognosis of disease are described. The methods segregate individual samples into distinct classes using quant. measurements of **expression** values for selected sets of genes in individual samples compared to a reference standard Samples displaying pos. and neg. correlations of the gene **expression** values with the reference standard samples exhibit distinct behaviors and pathohistol. features. Also disclosed are methods for identifying sets of genes whose **expression** patterns are correlated with a phenotype. Such sets are useful for characterizing cellular differentiation pathways and states and for identifying potential drug discovery targets. Panels for diagnosis and determination of risk of invasive and metastatic forms of lung, prostate and breast cancer are identified. Similarly, panels indicating recurrence of the cancers and poor prognostic outcomes are identified.

L10 ANSWER 3 OF 25 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 2004413839 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15194684
TITLE: **Expression** of the **human** myotonic dystrophy **kinase**-related Cdc42-binding **kinase** gamma is regulated by promoter DNA methylation and Sp1 binding.
AUTHOR: Ng Yvonne; Tan Ivan; Lim Louis; Leung Thomas
CORPORATE SOURCE: GSK-IMCB Group, Institute of Molecular and Cell Biology, 61 Biopolis Drive, Singapore 138673, Singapore.
SOURCE: Journal of biological chemistry, (2004 Aug 13) 279 (33) 34156-64.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200409
ENTRY DATE: Entered STN: 20040821
Last Updated on STN: 20040925
Entered Medline: 20040924

AB Myotonic dystrophy **kinase**-related Cdc42 binding **kinases** (MRCKs) are family members most related to the myotonic dystrophy **kinase** (DMPK), RhoA-binding **kinase** (ROK), and **citron kinase**. Two highly conserved members, MRCKalpha and -beta, have been previously identified and characterized. We now describe a novel isoform, MRCKgamma, which is functionally and structurally related to members of this **kinase** family. We show these **kinases** to have marked similarities in their genomic organization, substrate phosphorylation, and catalytic autoinhibition. Unlike MRCKalpha and -beta, which are **expressed** ubiquitously, MRCKgamma mRNA was only **expressed** in heart and skeletal muscle. In cultured cells, MRCKgamma showed differential **expression** with high levels of **expression** only in certain cell lines. DNA analysis showed that lack of **expression** is correlated with promoter DNA methylation. We have mapped the methylation sites in the MRCKgamma promoter. Significantly, agents that suppressed DNA methylation caused increases in the **expression** of the **kinase** in low-**expressing** cells, further supporting the notion that promoter DNA methylation plays an important role in the **expression** of MRCKgamma. Analysis of the MRCKgamma promoter has also revealed two proximal Sp1 sites that are essential for transcriptional activity. We conclude that both promoter DNA methylation and Sp1 binding are important regulators for MRCKgamma **expression**.

L10 ANSWER 4 OF 25 SCISEARCH COPYRIGHT (c) 2004 The Thomson Corporation. on STN
ACCESSION NUMBER: 2004:254053 SCISEARCH
THE GENUINE ARTICLE: 801PW
TITLE: Regulation of proteins affecting NMDA receptor-induced excitotoxicity in a Huntington's mouse model
AUTHOR: Jarabek B R; Yasuda R P; Wolfe B B (Reprint)
CORPORATE SOURCE: Georgetown Univ, Dept Pharmacol, 3900 Reservoir Rd NW, Washington, DC 20057 USA (Reprint); Georgetown Univ, Dept Pharmacol, Washington, DC 20057 USA
COUNTRY OF AUTHOR: USA
SOURCE: BRAIN, (MAR 2004) Vol. 127, Part 3, pp. 505-516.
Publisher: OXFORD UNIV PRESS, GREAT CLARENDON ST, OXFORD OX2 6DP, ENGLAND.
ISSN: 0006-8950.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 61

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Symptoms of Huntington's disease may be caused by a toxic insult triggered by the mutant **human** huntingtin (Htt) protein itself, by a maladaptive protective mechanism initiated in response to an insult, or by a combination of these. We observed a protection from N-methyl-D-aspartate (NMDA) receptor-induced excitotoxicity in striata of symptomatic N171-82Q mice, a new transgenic model of Huntington's disease. The goal of this study was to determine if NMDA receptor-mediated signalling pathways are altered in these mice. Multiple proteins of NMDA receptor and dopamine D1 receptor pathways are being regulated in ways predictive of the protection we observe. Although examining NMDA receptor subunit proteins showed no change in NR1, NR2A, or NR2B in the striata of the symptomatic mice, we observed a decrease in phosphorylation of NR1 at Ser(897), previously reported to decrease NMDA receptor current. The dopamine D1 receptor, responsible for protein **kinase** A activation and subsequent phosphorylation of Ser(897) of NR1, also showed an age-related decrease. Other proteins regulated in this disease were associated with PSD-95-like scaffolding proteins of the NMDA receptor. Specifically, we observed a decrease in membrane-associated neuronal nitric oxide synthase (nNOS), a decrease in PSD-95-like proteins, which link nNOS to the NMDA receptor complex, and a decrease in **citron** , a protein associated with dendritic spine formation. From these data, we conclude that the N171-82Q mice seem to be regulating, in a protective direction, many of the known effector pathways of NMDA receptor-induced excitotoxicity. These regulations, although seemingly effective in decreasing neuronal death, may in fact be causing some of the symptoms associated with the disease.

L10 ANSWER 5 OF 25 EMBASE
on STN

ACCESSION NUMBER: 2004430185 EMBASE
TITLE: Validating the prognostic value of marker genes derived from a non-small cell lung cancer microarray study.
AUTHOR: Blackhall F.H.; Wigle D.A.; Jurisica I.; Pintilie M.; Liu N.; Darling G.; Johnston M.R.; Keshavjee S.; Waddell T.; Winton T.; Shepherd F.A.; Tsao M.-S.
CORPORATE SOURCE: M.-S. Tsao, Div. of Cell. and Molecular Biology, University Health Network, Ontario Cancer Inst., Prncs. M., Toronto, Ont. M5G 2M9, Canada. Ming.Tsao@uhn.on.ca
SOURCE: Lung Cancer, (2004) 46/2 (197-204).
Refs: 17
ISSN: 0169-5002 CODEN: LUCAE5
PUBLISHER IDENT.: S 0169-5002(04)00155-2
COUNTRY: Ireland
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 016 Cancer
022 Human Genetics
LANGUAGE: English
SUMMARY LANGUAGE: English

AB We previously reported that our cDNA microarray analysis of primary non-small cell lung carcinoma (NSCLC) could predict for patients at increased risk of cancer recurrence. From the result of this analysis, we selected 11 genes that were considered candidate prognostic marker genes and used the realtime reverse transcription polymerase chain reaction (RT-PCR) to investigate their **expression** in the same set of NSCLC cases used in the microarray study. Cluster analysis of the realtime RT-PCR data separated these patients into two groups with significantly different disease-free survivals (log-rank test, P<0.017). In contrast, cluster analysis failed to confirm the prognostic significance of the realtime RT-PCR results for these 11 genes in a validation series of 92 NSCLC cases. In univariate analysis, hypoxia inducible factor 1α, Rho-GDP dissociation inhibitor (GDI) α (RhoGDI) and **Citron** /rho-interacting serine-threonine **kinase** 21 (**Citron** K21) were significant prognostic factors for disease-free survival in the

entire cohort of 130 NSCLC patients, but none were significant in multivariate analysis. The results demonstrate that the prognostic significance of microarray (SAM) results can be partially validated using realtime RT-PCR, but secondary validation using larger and independent series of tumors is necessary to identify true prognostic marker genes.

L10 ANSWER 6 OF 25 BIOTECHDS COPYRIGHT 2004 THE THOMSON CORP. on STN
DUPLICATE 2
ACCESSION NUMBER: 2003-11097 BIOTECHDS
TITLE: New **human citron** rho/rac-interacting **kinase**-short **kinase** polypeptide and polynucleotide for preventing or treating diseases associated with the polypeptide dysfunction, e.g. obesity or chronic obstructive pulmonary disease; **recombinant** protein production for use in disease therapy and gene therapy
AUTHOR: ZHU Z
PATENT ASSIGNEE: BAYER AG
PATENT INFO: WO 2003004629 16 Jan 2003
APPLICATION INFO: WO 2002-EP7229 1 Jul 2002
PRIORITY INFO: US 2002-375015 25 Apr 2002; US 2001-301853 2 Jul 2001
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2003-221595 [21]
AB DERWENT ABSTRACT:
NOVELTY - A new isolated polynucleotide (I) which encodes a **human citron** rho/rac-interacting **kinase**-short **kinase** polypeptide (II), is new.
DETAILED DESCRIPTION - A new isolated polynucleotide (I) selected from a polynucleotide: (a) which encodes a **human citron** rho/rac-interacting **kinase**-short **kinase** polypeptide (II) (which comprises a sequence of 495 (S3) or 497 (S4) amino acids fully defined in the specification, or a sequence that is at least 88% identical to S3 or S4); (b) which comprises a sequence of 1485 (S1) or 1765 (S2) bp given in the specification; (c) which hybridizes under stringent conditions to the polynucleotide in (a) and (b); (d) which has a sequence deviating from (a)-(c) due to the degeneration of the genetic code; and (e) which represents a fragment, derivative or allelic variation of (a)-(d). INDEPENDENT CLAIMS are also included for the following: (1) an **expression** vector containing the above polynucleotide; (2) a host cell comprising the **expression** vector; (3) a substantially purified **human citron** rho/rac-interacting **kinase**-short **kinase** polypeptide encoded by (I); (4) producing (II); (5) detecting the above polynucleotide or polypeptide; (6) a diagnostic kit for conducting method (5); (7) screening for agents which regulate or decrease the activity of the **citron** rho/rac-interacting **kinase**-short **kinase** polypeptide; (8) reducing the activity of **human citron** rho/rac-interacting **kinase**-short **kinase** polypeptide; (9) a reagent that modulates the activity of (II) or the polynucleotide cited above, which is identified by method (7); and (10) a pharmaceutical composition comprising the above **expression** vector or reagent, and a carrier.
BIOTECHNOLOGY - Preferred Method: Producing a **human citron** rho/rac-interacting **kinase**-short **kinase** polypeptide comprises culturing the host cell under conditions suitable for the **expression** of (II), and recovering the polypeptide from the host cell culture. Detecting the polynucleotide encoding the **human citron** rho/rac-interacting **kinase**-short **kinase** polypeptide in a biological sample, comprises hybridizing the above polynucleotide to a nucleic acid material of a biological sample to form a hybridization complex, and detecting the complex formed. Before hybridization, the nucleic acid material of the biological sample

is amplified. Detecting the above polynucleotide or polypeptide comprises contacting a biological sample with a reagent which specifically interacts with the polynucleotide or the polypeptide, and detecting the interaction. Screening for agents which decrease the activity of a **human citron** rho/rac-interacting **kinase**-short **kinase** polypeptide, comprises contacting a test compound with the above polypeptide or polynucleotide, and detecting the binding of the test compound to (II) or the polynucleotide, where a test compound which binds to the polypeptide or the polynucleotide is identified as a potential therapeutic agent for decreasing the activity of the **human citron** rho/rac-interacting **kinase**-short **kinase** polypeptide. In screening for agents which regulate the activity of the above polypeptide, the test compound is contacted with (II), and the activity of the **human citron** rho/rac-interacting **kinase**-short **kinase** polypeptide is detected, where the test compound which increases or decreases the **kinase** activity is identified as a potential therapeutic agent for increasing or decreasing the activity of the **kinase**. Reducing the activity of the **human citron** rho/rac-interacting **kinase**-short **kinase** comprises contacting a cell with a reagent which specifically binds to the above polypeptide or polynucleotide, where the activity of the **kinase** is reduced.

ACTIVITY - Anorectic; Antiinflammatory; Hypotensive; Antidiabetic; Cardiant; Antilipemic; Cerebroprotective; Antigout; Osteopathic; Antiarthritic; Cytostatic; Thrombolytic; Anticoagulant; Gynecological; Antidepressant. No biological data is given.

MECHANISM OF ACTION - Gene therapy.

USE - The polynucleotide and polypeptide are useful in preventing, ameliorating, or treating diseases associated with the polypeptide dysfunction. The **expression** vector or the reagent is useful in the preparation of a medicament for modulating the activity of a **human citron** rho/rac-interacting **kinase**-short **kinase** in a disease, such as obesity or chronic obstructive pulmonary disease (claimed). These may also be used for treating obesity/overweight-associated comorbidities, such as hypertension, diabetes, coronary artery disease, hyperlipidemia, stroke, gallbladder disease, gout, osteoarthritis, sleep apnea, cancer, thrombolic diseases, polycystic ovarian syndrome, reduced fertility, and depression. The polypeptide and polynucleotide are also useful in diagnostic assays or in genetic testing.

ADMINISTRATION - The dosage ranges from 0.1-100000 microg, up to a total dose of 1 g, depending upon the route of administration, which may be oral, parenteral (e.g. intravenous, intramuscular, intraarterial, subcutaneous), intramedullary, intrathecal, intraventricular, transdermal, intraperitoneal, intranasal, topical, sublingual, or rectal means.

EXAMPLE - No relevant example given. (73 pages)

L10 ANSWER 7 OF 25 BIOTECHDS COPYRIGHT 2004 THE THOMSON CORP. on STN
DUPLICATE 3

ACCESSION NUMBER: 2003-11086 BIOTECHDS

TITLE: New **human citron** rho/rac-interacting **kinase** (CRIK) polypeptide and polynucleotide, useful in preventing, ameliorating or treating diseases associated with **human** CRIK dysfunction, e.g. obesity, diabetes or Alzheimer's disease;
vector-mediated gene transfer and **expression** in host cell for **recombinant** protein production, drug screening and gene therapy

AUTHOR: ZHU Z

PATENT ASSIGNEE: BAYER AG

PATENT INFO: WO 2003004523 16 Jan 2003

APPLICATION INFO: WO 2002-EP7156 28 Jun 2002

PRIORITY INFO: US 2002-375014 25 Apr 2002; US 2001-301841 2 Jul 2001
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2003-221576 [21]
AB DERWENT ABSTRACT:

NOVELTY - An isolated polynucleotide (I) encoding a **human citron** rho/rac-interacting **kinase** polypeptide, comprising a 6165 or 8603 base pair sequence (S1), given in the specification, hybridizing under stringent conditions to them, deviating from them due to the degeneration of the genetic code, or a fragment, derivative or allelic variation of them, is new.

DETAILED DESCRIPTION - An isolated polynucleotide (I) encoding a **human citron** rho/rac-interacting **kinase** polypeptide, comprising a 6165 or 8603 base pair sequence (S1), given in the specification, hybridizing under stringent conditions to them, deviating from them due to the degeneration of the genetic code, or a fragment, derivative or allelic variation of them, is new. (I) encodes a 2054 residue amino acid sequence (S2), given in the specification, or amino acid sequences that are at least 97 % identical to the sequence of S2. INDEPENDENT CLAIMS are included for the following: (1) a substantially purified **human** CRIK polypeptide encoded by (I); (2) an **expression** vector containing (I); (3) a host cell containing the **expression** vector of (2); (4) producing a **human** CRIK polypeptide; (5) detecting a polynucleotide encoding a **human** CRIK polypeptide in a biological sample; (6) detecting (I) or a **human** CRIK polypeptide; (7) a diagnostic kit for conducting the method of (5) or (6); (8) screening for agents that regulate or decrease the activity of a **human** CRIK; (9) reducing the activity of **human** CRIK; (10) a reagent that modulates the activity of a **human** CRIK polypeptide or polynucleotide, where the reagent is identified by the method of (8); and (11) a pharmaceutical composition comprising the **expression** vector or the reagent, and a pharmaceutical carrier.

BIOTECHNOLOGY - Preparation: The polynucleotide can be made by a cell and isolated using standard nucleic acid purification techniques, or synthesized using an amplification technique, such as PCR, or by using an automatic synthesizer. Preferred Method: Producing a **human citron** rho/rac-interacting **kinase** (CRIK) polypeptide comprises culturing the host cell under conditions suitable for the **expression** of the polypeptide, and recovering the polypeptide from the host cell culture. Detecting a polynucleotide encoding a **human** CRIK polypeptide in a biological sample comprises hybridizing (I) to a nucleic acid material of a biological sample to form a hybridization complex, and detecting the hybridization complex formed. Before hybridization, the nucleic acid material of the biological sample is amplified. Detecting (I) or a **human** CRIK polypeptide comprises contacting a biological sample with a reagent that specifically interacts with the polynucleotide or the polypeptide, and detecting the interaction. Screening for agents that decrease the activity of a **human** CRIK comprises contacting a test compound with a **human** CRIK polypeptide encoded by (I), or with (I), and detecting binding of the test compound to the polypeptide or (I), where a test compound that binds to the polypeptide or polynucleotide is identified as a potential therapeutic agent for decreasing the activity of a **human** CRIK. Screening for agents that regulate the activity of a **human** CRIK comprises contacting a test compound with a **human** CRIK polypeptide encoded by (I), and detecting a **human** CRIK activity of the polypeptide, where a test compound that increases or decreases the **human** CRIK activity is identified as a potential therapeutic agent for increasing or decreasing, respectively, the activity of the **human** CRIK. Reducing the activity of **human** CRIK comprises contacting a cell with a reagent that specifically binds to **human** CRIK polypeptide or (I), where the activity of **human** CRIK is reduced.

ACTIVITY - Anorectic; Hypotensive; Cardiant; Antilipemic; Cerebroprotective; Antigout; Osteopathic; Antiarthritic; Cytostatic; Antidepressant; Immunomodulator; Antimanic; Tranquilizer; Antiparkinsonian; Nootropic; Neuroprotective; Antiinflammatory; Antidiabetic; Analgesic. No biological data is given.

MECHANISM OF ACTION - **Kinase** Inhibitor; **Kinase** Stimulator; Gene Therapy.

USE - The **human citron** rho/rac-interacting **kinase** (CRIK) polypeptide and polynucleotide are useful in preventing, ameliorating, or treating diseases associated with **human** CRIK dysfunction such as obesity and obesity-associated comorbidities (e.g. hypertension, coronary artery disease, hyperlipidemia, stroke, gout, osteoarthritis, some types of cancer including endometrial, breast, prostate and colon cancer), anorexia, cachexia, bulimia, central nervous system disorders (e.g. mood disorders, anxiety disorders, Parkinson's disease or Alzheimer's disease), chronic obstructive pulmonary disease, or diabetes. These can also be used to treat pain associated with the disorders. The **human** CRIK polypeptide is also useful in diagnostic assays or in genetic testing. The **expression** vector or the reagent is useful in preparing a medicament for modulating the activity of a **human** CRIK in a disease, e.g. obesity, a central nervous system disorder, or chronic obstructive pulmonary disease. (All claimed.) The fusion protein is useful for generating antibodies against CRIK polypeptide and for use in various assay systems. The methods are useful in producing and detecting the polynucleotide and polypeptide and in screening for agents that modulate the activity of the **human** CRIK polypeptide.

ADMINISTRATION - The dosage ranges from 0.1-100000 micro-g, up to a total dose of about 1g. Administration may be oral, intravenous, intramuscular, intra-arterial, subcutaneous, intramedullary, intrathecal, intraventricular, transdermal, intraperitoneal, intranasal, topical, sublingual, or rectal means.

EXAMPLE - No relevant example given.(237 pages)

L10 ANSWER 8 OF 25 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:	2003:837255 HCAPLUS
DOCUMENT NUMBER:	139:319351
TITLE:	Protein and cDNA sequences of a **human citron kinase** and diagnostic, and therapeutic use
INVENTOR(S):	Davison, Daniel B.; Feder, John N.; Lee, Liana M.; Ott, Karl-heinze
PATENT ASSIGNEE(S):	Bristol-Myers Squibb Company, USA
SOURCE:	PCT Int. Appl., 203 pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003087332	A2	20031023	WO 2003-US11189	20030411
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003220224	A1	20031127	US 2003-412897	20030411

PRIORITY APPLN. INFO.: US 2002-372745P P 20020412

AB The present invention provides protein and cDNA sequences of a **human citron kinase**. Also described are **expression** vectors, host cells, antisense mols., and antibodies associated with the protein **kinase** polynucleotide and/ or polypeptide of this invention. In addition, methods for treating, diagnosing, preventing, and screening for disorders or diseases associated with abnormal biol. activity of the protein **kinase** are described, as are methods for screening for modulators, e.g., agonists or antagonists, of the protein **kinase** activity and/or function.

L10 ANSWER 9 OF 25 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:282713 HCAPLUS

DOCUMENT NUMBER: 138:298904

TITLE: **Human** cDNA sequences and their encoded proteins and diagnostic and therapeutic uses

INVENTOR(S): Smithson, Glennda; Millet, Isabelle; Peyman, John A.; Kekuda, Ramesh; Ju, Jingfang; Li, Li; Guo, Xiaojia; Patturajan, Meera; Spytek, Kimberly A.; Edinger, Shlomit R.; Ellerman, Karen; Malyankar, Uriel M.; Ort, Tatiana; Gorman, Linda; Zerhusen, Bryan D.; Anderson, David W.; Zhong, Mei; Catterton, Elina; Ji, Weizhen; Miller, Charles E.; Rastelli, Luca; Stone, David J.; Pena, Carol E. A.; Shenoy, Suresh G.; Shimkets, Richard A.; Rothenberg, Mark E.; Leach, Martin D.; Agee, Michele L.; Berghs, Constance; Dipippo, Vincent A.; Eisen, Andrew J.; Gangolli, Esha A.; Rieger, Daniel K.; Spaderna, Steven K.

PATENT ASSIGNEE(S): Curagen Corporation, USA

SOURCE: PCT Int. Appl., 586 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 145

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003029424	A2	20030410	WO 2002-US31373	20021002
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004038223	A1	20040226	US 2002-262511	20021001
US 2004038877	A1	20040226	US 2002-262839	20021001

PRIORITY APPLN. INFO.:

US 2001-326483P	P	20011002
US 2001-327435P	P	20011005
US 2001-327449P	P	20011005
US 2001-327917P	P	20011009
US 2001-328029P	P	20011009
US 2001-328044P	P	20011009
US 2001-328056P	P	20011009
US 2001-328849P	P	20011012
US 2001-329414P	P	20011015
US 2001-330142P	P	20011017
US 2001-330309P	P	20011018
US 2001-341058P	P	20011022
US 2001-339266P	P	20011024

US 2001-343629P	P	20011024
US 2001-349575P	P	20011029
US 2001-346357P	P	20011101
US 2002-373260P	P	20020417
US 2002-373815P	P	20020419
US 2002-373817P	P	20020419
US 2002-373826P	P	20020419
US 2002-373884P	P	20020419
US 2002-374977P	P	20020422
US 2002-381037P	P	20020516
US 2002-381038P	P	20020516
US 2002-381042P	P	20020516
US 2002-381642P	P	20020517
US 2002-383656P	P	20020528
US 2002-383831P	P	20020529
US 2002-391335P	P	20020625
US 2002-262511	A2	20021001
US 2001-327342P	P	20011005
US 2002-371972P	P	20020412
US 2002-371980P	P	20020412
US 2002-373261P	P	20020417
US 2002-373805P	P	20020419
US 2002-374738P	P	20020423
US 2002-381101P	P	20020516
US 2002-381635P	P	20020517
US 2002-383830P	P	20020529

AB Disclosed herein are 55 cDNA sequences that encode novel **human** polypeptides that are members of various protein families. The NOV55a gene is a Na+-dependent neutral amino acid transporter that exhibits high affinity electroneutral uptake of neutral amino acids, is localized to the plasma membrane, and whose **expression** pattern and function is an indication of a role in obesity and/or diabetes. Also disclosed are polypeptides encoded by these nucleic acid sequences, and antibodies, which immunospecifically-bind to the polypeptide, as well as derivs., variants, mutants, or fragments of the aforementioned polypeptide, polynucleotide, or antibody. The invention further discloses therapeutic, diagnostic and research methods for diagnosis, treatment, and prevention of disorders involving any one of these novel **human** nucleic acids and proteins.

L10 ANSWER 10 OF 25 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:177125 HCAPLUS
DOCUMENT NUMBER: 138:216597
TITLE: Differentially **expressed** nucleic acids and their encoded proteins associated with pain and their use in screening for regulatory agents
INVENTOR(S): Woolf, Clifford; D'Urso, Donatella; Befort, Katia; Costigan, Michael
PATENT ASSIGNEE(S): The General Hospital Corporation, USA; Bayer AG
SOURCE: PCT Int. Appl., 1017 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003016475	A2	20030227	WO 2002-XF25765	20020814

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA,

UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

WO 2003016475 A2 20030227 WO 2002-US25765 20020814
WO 2003016475 A3 20040910
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2001-312147P P 20010814
US 2001-346382P P 20011101
US 2001-333347P P 20011126
WO 2002-US25765 A 20020814

AB The present invention relates to **human** and rat nucleic acid sequences which are related to pain and which are differentially **expressed** during pain. The nucleic acids are differentially **expressed** by at least ±1.4-fold in any or all of the following conditions using the Affymetrix **human** U95, murine U74 and rat U34 GeneChip arrays: axotomy, spared nerve injury, chronic construction, spinal segmental nerve lesion, and inflammatory pain models. The invention further relates to methods of identifying nucleic acid sequences which are differentially **expressed** during pain, microarrays comprising such differentially **expressed** sequences, and methods of screening agents for the ability to regulate the **expression** of such differentially **expressed** sequences. [This abstract record is one of seven records for this document necessitated by the large number of index entries required to fully index the document and publication system constraints.].

L10 ANSWER 11 OF 25 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:117955 HCAPLUS
DOCUMENT NUMBER: 138:165725
TITLE: Protein, gene and cDNA sequences of a novel **human citron kinase** and their uses in drug screening
INVENTOR(S): Wei, Ming-Hui; Chaturvedi, Kabir; Di Francesco, Valentina; Beasley, Ellen M.
PATENT ASSIGNEE(S): Applera Corporation, USA
SOURCE: PCT Int. Appl., 105 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003012034	A2	20030213	WO 2002-US23268	20020723
WO 2003012034	A3	20031016		
WO 2003012034	C2	20040304		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,

UA, UG, US, UZ, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 6638745	B1	20031028	US 2001-916204	20010727
EP 1419242	A2	20040519	EP 2002-791541	20020723

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK

PRIORITY APPLN. INFO.:	US 2001-916204	A 20010727
	US 2001-804471	A2 20010313
	WO 2002-US23268	W 20020723

AB The invention provides protein, cDNA and genomic sequences for a novel **human citron kinase**. Specifically, a virtual northern blot shows **citron kinase** gene **expression** in liver, proliferating erythroid cells of blood, and glioblastomas of the brain. Thirteen single nucleotide polymorphisms have been found on **citron kinase** gene that has been mapped to **human** chromosome 12. The invention also relates to screening for **citron kinase** modulators and their uses in therapy. The invention further relates to methods, vector and hosts for **expression** of **citron kinase** .

L10 ANSWER 12 OF 25 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:	2003:851250 HCAPLUS
DOCUMENT NUMBER:	139:346785
TITLE:	**Cloning**, sequence and characterization of a **human citron kinase** homolog gene
INVENTOR(S):	Wei, Ming-Hui; Chaturvedi, Kabir; DiFrancesco, Valentina; Beasley, Ellen M.
PATENT ASSIGNEE(S):	Applera Corporation, USA
SOURCE:	U.S., 78 pp., Cont.-in-part of U.S. Ser. No. 804,471. CODEN: USXXAM
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	3

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6638745	B1	20031028	US 2001-916204	20010727
US 2002132322	A1	20020919	US 2001-804471	20010313
US 6479269	B2	20021112		
WO 2003012034	A2	20030213	WO 2002-US23268	20020723
WO 2003012034	A3	20031016		
WO 2003012034	C2	20040304		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

EP 1419242	A2	20040519	EP 2002-791541	20020723

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK

US 2003049795	A1	20030313	US 2002-282048	20021029
US 6692948	B2	20040217		

PRIORITY APPLN. INFO.:	US 2001-804471	A2 20010313
	US 2001-916204	A 20010727

WO 2002-US23268 W 20020723

AB The cDNA and genomic sequences and the encoded amino acid sequence of a **human kinase** that is related to the **citron kinase** subfamily are provided. Chromosomal mapping of the **citron kinase** homolog gene, tissue-specific **expression** profile and structural motifs of the polypeptide are provided. Intron/exon structure and SNPs of the **citron kinase** homolog gene are also identified. The present invention specifically provides isolated peptide and nucleic acid mols., methods of identifying orthologs and paralogs of the **kinase** peptides, and methods of identifying modulators of the **kinase** peptides.

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 13 OF 25 MEDLINE on STN
ACCESSION NUMBER: 2003040917 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12411428
TITLE: **Citron kinase** is a cell cycle-dependent, nuclear protein required for G2/M transition of hepatocytes.
AUTHOR: Liu Huifei; Di Cunto Ferdinando; Imarisio Sara; Reid Lola M
CORPORATE SOURCE: Department of Cell and Molecular Physiology, University of North Carolina School of Medicine, Chapel Hill, 27599, USA.
CONTRACT NUMBER: 1 R01 DK52851 (NIDDK)
SOURCE: Journal of biological chemistry, (2003 Jan 24) 278 (4) 2541-8.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200303
ENTRY DATE: Entered STN: 20030129
Last Updated on STN: 20030305
Entered Medline: 20030304

AB **Citron Kinase** (**Citron**-K) is a cell cycle-dependent protein regulating the G(2)/M transition in hepatocytes. Synchronization studies demonstrated that **expression** of the **Citron**-K protein starts at the late S and/or the early G(2) phase after that of cyclin B1. **Expression** of **Citron**-K is developmentally regulated. Levels of **Citron**-K mRNA and protein are highest in embryonic liver and gradually decrease after birth. **Citron**-K exists in interphase nuclei and begins to disperse into the cytoplasm at prophase. It concentrates at the cleavage furrow and midbody during anaphase, telophase, and cytokinesis, implicating a role in the control of cytokinesis. However, studies with knockouts show that **Citron**-K is not essential for cytokinesis in hepatocytes. Instead, loss of **Citron**-K causes a significant increase of G(2) tetraploid nuclei in one-week-old rat and mouse liver. In addition, **Citron**-K deficiency triggers apoptosis in a small subset of embryonic liver cells. In summary, our data demonstrate that **Citron**-K has a distinct cell cycle-dependent **expression** pattern and cellular localization as a downstream target of Rho-GTPase and functions in the control of G(2)/M transition in the hepatocyte cell cycle.

L10 ANSWER 14 OF 25 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:786041 HCAPLUS
DOCUMENT NUMBER: 139:362827
TITLE: Altered **expression** of genes involved in hepatic morphogenesis and fibrogenesis are identified by cDNA microarray analysis in biliary atresia
AUTHOR(S): Chen, Limin; Goryachev, Andrew; Sun, Jin; Kim, Peter; Zhang, Hui; Phillips, M. James; Macgregor, Pascale;

Lebel, Sylvie; Edwards, Aled M.; Cao, Qiongfang; Furuya, Katryn N.

CORPORATE SOURCE: Banting and Best Department of Medical Research, Faculty of Medicine, University of Toronto, Toronto, ON, Can.

SOURCE: Hepatology (Philadelphia, PA, United States) (2003), 38(3), 567-576
CODEN: HPTLD9; ISSN: 0270-9139
PUBLISHER: W. B. Saunders Co.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Biliary atresia (BA) is characterized by a progressive, sclerosing, inflammatory process that leads to cirrhosis in infancy. Although it is the most common indication for liver transplantation in early childhood, little is known about its etiopathogenesis. To elucidate factors involved in this process, we performed comprehensive genome-wide gene **expression** anal. using cDNA microarrays. The authors compared mRNA **expression** levels of approx. 18,000 **human** genes from normal, diseased control, and end-stage BA livers. Reverse-transcription polymerase chain reaction (RT-PCR) and Northern blot anal. were performed to confirm changes in gene **expression**. Cluster and principal component anal. showed that all BA samples clustered together, forming a distinct group well separated from normal and diseased controls. We further identified 35 genes and ESTs whose **expression** differentiated BA from normal and diseased controls. Most of these genes are known to be associated with cell signaling, transcription regulation, hepatic development, morphogenesis, and fibrogenesis. In conclusion, this study serves to delineate processes that are involved in the pathogenesis of BA.

REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 15 OF 25 SCISEARCH COPYRIGHT (c) 2004 The Thomson Corporation. on STN

ACCESSION NUMBER: 2003:196119 SCISEARCH
THE GENUINE ARTICLE: 647ZT

TITLE: Genomic organization of **human** myotonic dystrophy **kinase**-related Cdc42-binding **kinase** alpha reveals multiple alternative splicing and functional diversity

AUTHOR: Tan I; Cheong A; Lim L; Leung T (Reprint)

CORPORATE SOURCE: Glaxo, IMCB Grp, Inst Mol & Cell Biol, 30 Med Dr, Singapore 117609, Singapore (Reprint); Glaxo, IMCB Grp, Inst Mol & Cell Biol, Singapore 117609, Singapore; UCL, Neurol Inst, Dept Mol Pathogenesis, London WC1N 1PJ, England

COUNTRY OF AUTHOR: Singapore; England

SOURCE: GENE, (30 JAN 2003) Vol. 304, pp. 107-115.
Publisher: ELSEVIER SCIENCE BV, PO BOX 211, 1000 AE AMSTERDAM, NETHERLANDS.
ISSN: 0378-1119.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 36

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Myotonic dystrophy **kinase**-related Cdc42-binding **kinase** alpha (MRCKalpha) is a Cdc42/Rac interactive binding-containing serine/threonine **kinase** with multiple functional domains. Its roles in the regulation of peripheral actin reorganization in HeLa cells and NGF-induced neurite outgrowth in PC12 cells have been documented. Here we report the characterization of the genomic structure and alternative splicing of the **human** counterpart. **Human** MRCKalpha gene is located on chromosome 1q42.1, spanning a genomic region of 250-300 kb and is composed of 41

exons. Four exons in the internal variable region and six in the 3' end were found to undergo extensive alternative splicing, giving rise to 96 possible transcripts of different combinations. The region of the internal splice site that defines a variable region in between two functional domains of opposite regulatory effects on MRCKalpha catalytic activity, and the 3' end splice site that generates variants with differential GTPase binding activity suggest a role for these alternative splicing events in MRCKa regulation. (C) 2002 Elsevier Science B.V. All rights reserved.

L10 ANSWER 16 OF 25 BIOTECHDS COPYRIGHT 2004 THE THOMSON CORP. on STN
DUPLICATE 4
ACCESSION NUMBER: 2003-01894 BIOTECHDS
TITLE: Novel polynucleotide encoding **human** proteins that are structurally similar to animal **kinases**, useful for drug screening, diagnosis, in gene therapy of disorders and diseases e.g. cancer and pharmacogenomic applications; **recombinant** enzyme protein production and sense and antisense sequence use in disease therapy and gene therapy
AUTHOR: YU X; MIRANDA M; FRIDDLE C J
PATENT ASSIGNEE: LEXICON GENETICS INC
PATENT INFO: WO 2002059325 1 Aug 2002
APPLICATION INFO: WO 2001-US50497 20 Dec 2001
PRIORITY INFO: US 2000-258335 27 Dec 2000; US 2000-258335 27 Dec 2000
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2002-599796 [64]
AB DERWENT ABSTRACT:
NOVELTY - An isolated nucleic acid molecule (I) comprising a nucleotide sequence encoding a novel **human** protein (NHP) of 2054 (S1) or 1958 (S2) amino acids given in specification, that share structural similarity with animal **kinases**, including serine-threonine **kinases**, particularly **Citron** rho-interacting **kinases**, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for: (1) an isolated nucleic acid molecule (II) comprising a nucleotide sequence that encodes (S1) and hybridizes under stringent conditions to a sequence (S3) of 6165 base pairs given in the specification, or its complement; and (2) an isolated nucleic acid molecule (III) comprising at least 24 contiguous bases of (S3).

WIDER DISCLOSURE - Disclosed are: (1) novel **human** proteins (NHPs) encoded by (I), that share structural similarity with animal **kinases**; (2) host cell **expressing** systems comprising (I); (3) antibodies to NHP and anti-idiotypic antibodies; (4) fusion proteins comprising NHP; (5) genetically engineered animals that either lack or over **express** (I); (6) antagonists and agonists of NHP; (7) compounds that modulate the **expression** or activity NHP which can be used for diagnosis, drug screening, clinical trial monitoring, treatment of diseases and disorders, and cosmetic or nutriceutical applications; (8) identifying compounds that modulate, **expression** and/or activity of NHP; (9) degenerate nucleic acid variants of (I); (9) vectors that contain (I); (10) nucleotide sequences (e.g. antisense and ribozyme molecules) that inhibit **expression** of (I); and (11) proteins that are functionally equivalent to NHPs.

BIOTECHNOLOGY - Preferred Protein: NHPs are novel proteins **expressed** in **human** cell lines and **human** testis, small intestine, fetal kidney, adenocarcinoma, embryonic carcinoma cells and osteosarcoma cells.

ACTIVITY - Nootropic; Cytostatic.

MECHANISM OF ACTION - Gene therapy. No suitable data given.

USE - NHP oligonucleotides are useful as hybridization probes for screening libraries and assessing gene **expression** patterns. NHP sequences are useful to identify mutations associated with a particular

disease and also as a diagnostic or prognostic assay, and also in the molecular mutagenesis/evolution of proteins that are at least partially encoded by the NHP sequences. Sequences derived from regions adjacent to the intron/exon boundaries of NHP gene can be used to design primers for use in amplification assays to detect mutations within the exons, splice sites, introns that can be used in diagnostics and pharmacogenomics. NHP sequences are utilized in microarrays or other assay formats, to screen collections of genetic material from patients who have a particular medical condition. NHP nucleotide sequences are useful for drug screening effective in the treatment of symptomatic or phenotypic manifestations of perturbing the normal function of NHP in the body, and nucleotide constructs encoding NHP products are used to genetically engineer host cells to **express** NHP products in vivo. These genetically engineered cells function as bioreactors in the body delivering a continuous supply of a NHP, a NHP peptide, or a NHP fusion protein to the body. Nucleotide construct encoding NHP products are also useful in gene therapy for modulating NHP **expression** and to produce genetically engineered host cells to **express** NHP products in vivo. NHP nucleotide sequences may also be used as part of ribozyme and/or triple helix sequences that are useful for NHP gene regulation. The encoded NHP polypeptides are useful for generating antibodies, as reagents in diagnostic assays, for identifying other cellular gene products related to NHP and as reagents in assays for screening for compounds that are useful in the treatment of mental, biological or medical disorders and diseases including cancer. (50 pages)

L10 ANSWER 17 OF 25 BIOTECHDS COPYRIGHT 2004 THE THOMSON CORP. on STN
DUPLICATE 5
ACCESSION NUMBER: 2002-18283 BIOTECHDS
TITLE: Novel isolated NOVX polypeptides and polynucleotides homologous to attractin, plexin, papin-like family of proteins, useful for treating atherosclerosis, diabetes, cancer, Alzheimer's disease, hemophilia and stroke; **recombinant** protein production and sense and antisense sequence use in disease therapy and gene therapy
AUTHOR: GERLACH V L; MACDOUGALL J R; SMITHSON G; MILLET I; STONE D; GUNTHER E; ELLERMAN K; GROSSE W M; ALSOBROOK J P; LEPLEY D M; BURGESS C E; PADIGARU M; KEKUDA R; SPYTEK K A; LEACH M D; SHIMKETS R A
PATENT ASSIGNEE: CURAGEN CORP
PATENT INFO: WO 2002026826 4 Apr 2002
APPLICATION INFO: WO 2000-US42336 27 Sep 2000
PRIORITY INFO: US 2001-235631 26 Sep 2001
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: WPI: 2002-499860 [53]
AB DERWENT ABSTRACT:
NOVELTY - An isolated NOVX polypeptide (I) comprising an amino acid sequence of mature form of sequence or amino sequence (S) of 841, 837, 1185, 2066, 2053, 1896, 480, 879, 442, 2814 or 2811 amino acids fully defined in specification or a variant of the above that differs not more than 15% of amino acid residues, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following: (1) an isolated nucleic acid molecule (II) comprising a nucleic acid sequence encoding (I); a nucleic acid fragment encoding a portion of a polypeptide comprising (S1) or its variant that differs not more than 15% of amino acid residues and a nucleic acid molecule comprising the complement of the above; (2) a vector (III) comprising (II); (3) an antibody (IV) that binds specifically to (I); (4) a cell (V) comprising (III); (5) modulating the activity of (I) comprising contacting a cell sample **expressing** (I) with a compound that binds to (I); (6) a pharmaceutical composition (VI) comprising (I), (II) or (IV); and (7) a kit comprising (VI), in one or more containers.

WIDER DISCLOSURE - The following are also disclosed: (1)

immunoconjugates comprising (IV) conjugated to a cytotoxic agent;(2) derivatives, analogs and homologs of (II); (3) NOVX chimeric or fusion proteins, useful therapeutically, in purification of NOVX ligands, producing anti-NOVX antibodies, and in screening assays; (4) isolated antisense nucleic acids that are hybridizable or complementary to (II); and (5) a kit for detecting presence of NOVX in a sample.

BIOTECHNOLOGY - Preparation: (I) is produced by **recombinant** DNA techniques. Preferred Polypeptide: In (I), the amino acid sequence of the variant comprises a conservative amino acid substitution. (I) comprises the amino acid sequence of a naturally occurring allelic variant of (S1) i.e. the translation of a nucleic acid sequence differing by a single nucleotide from a nucleic acid sequence (S2) of 2838, 2526, 2531, 3609, 6201, 6189, 5691, 1535, 2657, 1366, 1421, 2024, 8640 or 8640 nucleotides fully defined in the specification. NOV1 is homologous to a insulin like growth factor binding protein complex-acid labile subunit-like family of proteins, NOV2 is homologous to attractin-like family of proteins, and NOV3 is homologous to a family of RHO/RAC-interacting **citron kinase**-like proteins. NOV4 is homologous to the plexin-like family of proteins, NOV5 is homologous to the dopamine receptor-like family of proteins, and NOV6 is homologous to the metabotropic glutamate receptor-like family of proteins. NOV7 is homologous to members of PV-like family of proteins, and NOV8 is homologous to papin-like family of proteins. Preferred Nucleic Acid: (II) comprises the nucleotide sequence of a naturally occurring allelic nucleic acid variant, and encodes a polypeptide comprising the amino acid sequence of a naturally occurring polypeptide variant. (II) comprises a nucleotide sequence of (S2) or a sequence differing by one or more nucleotides from (S2) but does not differ more than 20% of the nucleotides and a nucleic acid fragment of the above. (II) hybridizes to (S2) or to its complement. In (II), the nucleic acid molecule comprises a sequence of a first nucleotide sequence comprising a coding sequence differing by one or more nucleotide sequences from a coding sequence encoding the amino acid sequence, provided that not more than 20% of the nucleotides in the coding sequence in the first nucleotide sequence differ from the coding sequence; an isolated second polynucleotide complementary to the first polynucleotide; and a nucleic acid fragment of the above. Preferred Vector: (III) further comprising a promoter operably-linked to the nucleic acid molecule.

ACTIVITY - Cytostatic; Uropathic, Gynecological; Hepatotropic; Antiinflammatory; Antiinfertility; Antilipemic; Antiarteriosclerotic; Hypotensive; Dermatological; Hemostatic; Anorectic; Antidiabetic; Immunosuppressive; Antiasthmatic; Antipsoriatic; Antiallergic; Nootropic; Neuroprotective; Cerebroprotective; Antiparkinsonian; Anticonvulsant; Tranquilizer; Analgesic; Neuroleptic; Antialcoholic; Nephrotropic. No supporting data given.

MECHANISM OF ACTION - Modulator of **expression** of NOVX polypeptide; Gene therapy; Vaccine. No supporting data given.

USE - (I), (II) or (IV) is useful in treating or preventing a NOVX-associated disorder which is cardiomyopathy, atherosclerosis and diabetes in a **human**, where the disorder is related to cell signal processing and metabolic pathway modulation. (IV) is useful for determining the presence or amount of (I) in a sample. Fragment of (I) is useful as probe for determining the presence or amount of (II) in the sample. The presence or amount of (II) is useful as a marker for cancerous cell or tissue type. (I) is useful for identifying an agent which is cellular receptor or downstream effector. (I) is also useful for identifying an agent that modulates the **expression** or activity of (I). (I) or (II) is useful for determining the presence or predisposition to a disease associated with altered levels of (I) or (II), especially cancer. Polypeptide 95% identical to (I) or its biologically active fragment, or (IV) is useful for treating a pathological state in a mammal (claimed). (I) is useful as immunogen to produce (IV), and as vaccines and is also useful in screening for potential agonist and antagonist compounds. (I) is useful for screening

for a modulator of activity or of latency or predisposition to disorders. Fragments of (I) (cDNA) sequence useful in chromosome mapping, tissue typing and in forensic identification of a biological sample. Probes obtained from (II) is useful for detecting transcripts or genomic sequences encoding the same or homologous proteins and identifying cells or tissues that misexpress an NOVX protein. (II) is useful in gene therapy, and in purification of (I). (II) is useful to **express** NOVX protein, to detect NOVX mRNA or a genetic lesion in an NOVX gene and to modulate NOVX activity. (I) or (II) is useful for prognostic (predictive) assays, for prophylactically treating an individual. Agent that modulate NOVX **expression** is useful for preventing or treating diseases. (I), (II) or (III) is useful in treating diseases such as hypertension, congenital heart defects, aortic stenosis, obesity, infectious disease, anorexia, cancer, Alzheimer's disease, Parkinson's disorders, neurodegenerative disorders, hemophilia, dyslipidemias, hematopoietic diseases, scleroderma, fertility, idiopathic thrombocytopenic purpura, graft versus host diseases, Crohn's disease, multiple sclerosis, cirrhosis, autoimmune disease, systemic lupus erythematosus, asthma, arthritis, psoriasis, allergy, stroke, anxiety, Lesch-Nyhan syndrome, schizophrenia, cerebellar ataxia, pain and alcoholism. (IV) is useful to detect and isolate NOVX proteins and modulate NOVX activity. (V) is useful to produce non-**human** transgenic animals which is useful for studying the function and/or activity of NOVX protein and for identifying and/or evaluating modulators of NOVX protein activity.

ADMINISTRATION - Administered by parenteral, oral, transdermal, transmucosal or rectal route. No dosage is given.

EXAMPLE - The polymerase chain reaction (PCR) primers used were primer 1: (5'-3') NOVIC: TCATCACATGACAACATGAAGCTGT and NOV7a: CCAATCTCTGATGCCCTGCGAT, primer 2 (5'-3') NOVIC: GAAAGCCCTCAAACTCTCCATCTATG and NOV7a: AGGTCAGTGCCGGAGCCTCC. These primers were designed based on silico predictions for the full length cDNA, part (one or more exons) of the DNA or protein sequence of the target sequence or by translated homology of the predicted exons to closely related **human** sequences from other species. These primers were then employed in PCR amplification based on the pool of **human** cDNAs like adrenal gland, bone marrow, brain-whole fetal brain, pancreas, pituitary gland, placenta, prostate, salivary gland, skeletal muscle, small intestine, spinal cord, spleen, stomach, testis, thyroid, trachea and uterus. The resulting amplicons were gel purified, **cloned** and sequenced to high redundancy. The PCR product derived from exon linking was **cloned** into the PCR2.1 vector. The resulting bacterial **clone** had an insert covering the entire open reading frame **cloned** into the PCR2.1 vector. The resulting sequences from all **clones** were assembled with themselves, with other fragments in CuraGen Corporations database and with public **expressed** sequence tags (ESTs). Fragment and ESTs were included as components for an assembly when the extent of the identity with another component of the assembly was 95% over 50 bp. Sequence traces were evaluated manually and edited for corrections. Thus, the sequences encoding the full length NOVX protein of 841, 837, 1185, 2066, 2053, 1896, 480, 879, 442, 2814 or 2811 amino acids defined in the specification, was obtained. (308 pages)

L10 ANSWER 18 OF 25 HCAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:	2002:716956 HCAPLUS
DOCUMENT NUMBER:	137:259346
TITLE:	Identification, **cloning**, genomic and cDNA sequences and use of **human citron kinase** family member
INVENTOR(S):	Webster, Marion; Yan, Chunhua; Di Francesco, Valentina; Beasley, Ellen M.
PATENT ASSIGNEE(S):	USA
SOURCE:	U.S. Pat. Appl. Publ., 184 pp.

CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002132322	A1	20020919	US 2001-804471	20010313
US 6479269	B2	20021112		
US 6638745	B1	20031028	US 2001-916204	20010727
US 2003022340	A1	20030130	US 2002-238709	20020911
US 6680188	B2	20040120		
US 2003049795	A1	20030313	US 2002-282048	20021029
US 6692948	B2	20040217		
US 2004091993	A1	20040513	US 2003-724594	20031202

PRIORITY APPLN. INFO.:
US 2001-804471 A2 20010313
US 2001-916204 A3 20010727
US 2002-238709 A3 20020911

AB The present invention provides amino acid sequences of peptides that are encoded by genes within the **human** genome, the **kinase** peptides of the present invention. The cDNA sequence and the encoded amino acid sequence of the **human kinase** that is related to the rho/rac-interacting **citron kinase** (CRIK) subfamily are provided. Chromosomal mapping of the **citron kinase** gene, tissue-specific **expression** profiles, and structural motifs of the polypeptide are provided. The genomic sequence of the **citron kinase** gene and SNPs that have been found in the gene are disclosed. The present invention specifically provides isolated peptide and nucleic acid mols., methods of identifying orthologs and paralogs of the **citron kinase** peptides, and methods of identifying modulators of the **citron kinase** peptides.

L10 ANSWER 19 OF 25 SCISEARCH COPYRIGHT (c) 2004 The Thomson Corporation. on STN
ACCESSION NUMBER: 2002:556330 SCISEARCH
THE GENUINE ARTICLE: 566VF
TITLE: Nir2, a **human** homolog of Drosophila melanogaster retinal degeneration B protein, is essential for cytokinesis
AUTHOR: Litvak V; Tian D H; Carmon S; Lev S (Reprint)
CORPORATE SOURCE: Weizmann Inst Sci, Dept Neurobiol, IL-76100 Rehovot, Israel (Reprint)
COUNTRY OF AUTHOR: Israel
SOURCE: MOLECULAR AND CELLULAR BIOLOGY, (JUL 2002) Vol. 22, No. 14, pp. 5064-5075.
Publisher: AMER SOC MICROBIOLOGY, 1752 N ST NW, WASHINGTON, DC 20036-2904 USA.
ISSN: 0270-7306.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 63

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Cytokinesis, the final stage of eukaryotic cell division, ensures the production of two daughter cells. It requires fine coordination between the plasma membrane and cytoskeletal networks, and it is known to be regulated by several intracellular proteins, including the small GTPase Rho and its effectors. In this study we provide evidence that the protein Nir2 is essential for cytokinesis. Microinjection of anti-Nir2 antibodies into interphase cells blocks cytokinesis, as it results in the production of multinucleate cells. Immunolocalization studies revealed that Nir2 is mainly localized in the Golgi apparatus in interphase cells, but it is recruited to the cleavage furrow and the midbody during cytokinesis. Nir2

colocalizes with the small GTPase RhoA in the cleavage furrow and the midbody, and it associates with RhoA in mitotic cells. Its N-terminal region, which contains a phosphatidylinositol transfer domain and a novel Rho-inhibitory domain (Rid), is required for normal cytokinesis, as overexpression of an N-terminal-truncated mutant blocks cytokinesis completion. Time-lapse videomicroscopy revealed that this mutant normally initiates cytokinesis but fails to complete it, due to cleavage furrow regression, while Rid markedly affects cytokinesis due to abnormal contractility. Rid-**expressing** cells exhibit aberrant ingression and ectopic cleavage sites; the cells fail to segregate into daughter cells and they form a long unseparated bridge-like cytoplasmic structure. These results provide new insight into the cellular functions of Nir2 and introduce it as a novel regulator of cytokinesis.

L10 ANSWER 20 OF 25 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:501939 HCAPLUS
DOCUMENT NUMBER: 137:199252
TITLE: Gene **expression** patterns in **human** liver cancers
AUTHOR(S): Chen, Xin; Cheung, Siu Tim; So, Samuel; Fan, Sheung Tat; Barry, Christopher; Higgins, John; Lai, Kin-Man; Ji, Jiafu; Dudoit, Sandrine; Ng, Irene O. L.; Van de Rijn, Matt; Botstein, David; Brown, Patrick O.
CORPORATE SOURCE: Department of Biochemistry, Howard Hughes Medical Institute, Stanford University School of Medicine, Stanford, CA, 94305, USA
SOURCE: Molecular Biology of the Cell (2002), 13(6), 1929-1939
CODEN: MBCEEV; ISSN: 1059-1524
PUBLISHER: American Society for Cell Biology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Hepatocellular carcinoma (HCC) is a leading cause of death worldwide. Using cDNA microarrays to characterize patterns of gene **expression** in HCC, we found consistent differences between the **expression** patterns in HCC compared with those seen in nontumor liver tissues. The **expression** patterns in HCC were also readily distinguished from those associated with tumors metastatic to liver. The global gene **expression** patterns intrinsic to each tumor were sufficiently distinctive that multiple tumor nodules from the same patient could usually be recognized and distinguished from all the others in the large sample set on the basis of their gene **expression** patterns alone. The distinctive gene **expression** patterns are characteristic of the tumors and not the patient; the **expression** programs seen in **clonally** independent tumor nodules in the same patient were no more similar than those in tumors from different patients. Moreover, **clonally** related tumor masses that showed distinct **expression** profiles were also distinguished by genotypic differences. Some features of the gene **expression** patterns were associated with specific phenotypic and genotypic characteristics of the tumors, including growth rate, vascular invasion, and p53 over-**expression**.
REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 21 OF 25 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:763058 HCAPLUS
DOCUMENT NUMBER: 135:327323
TITLE: NMDA receptor complexes for diagnostic and therapeutic use
INVENTOR(S): Grant, Seth Garran Niels; Husi, Holger
PATENT ASSIGNEE(S): The University Court of the University of Edinburgh, UK
SOURCE: PCT Int. Appl., 202 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001077170	A2	20011018	WO 2001-GB1570	20010406
WO 2001077170	A3	20020328		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2405311	AA	20011018	CA 2001-2405311	20010406
EP 1272517	A2	20030108	EP 2001-917331	20010406
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2003530125	T2	20031014	JP 2001-575640	20010406
US 2003176651	A1	20030918	US 2003-240873	20030310
PRIORITY APPLN. INFO.:			GB 2000-8321 A	20000406
			WO 2001-GB1570 W	20010406

AB The present invention provides multi-protein complexes, and sub-complexes thereof, and methods of producing the same. Preferably, the complexes comprise an NMDA receptor. The present invention further provides methods of identifying a compound for treating disorders and conditions associated with dysfunction of NMDA receptors in the central nervous system. Addnl., there are provided methods of diagnosing or aiding diagnosis of disorders and conditions associated with dysfunction of NMDA receptors in the central nervous system.

L10 ANSWER 22 OF 25 MEDLINE on STN DUPLICATE 6
ACCESSION NUMBER: 2001563963 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11591816
TITLE: Rho-dependent transfer of **Citron-kinase** to the cleavage furrow of dividing cells.
AUTHOR: Eda M; Yonemura S; Kato T; Watanabe N; Ishizaki T; Madaule P; Narumiya S
CORPORATE SOURCE: Department of Pharmacology, Kyoto University Faculty of Medicine, Sakyo, Kyoto 606-8501, Japan.
SOURCE: Journal of cell science, (2001 Sep) 114 (Pt 18) 3273-84. Journal code: 0052457. ISSN: 0021-9533.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200112
ENTRY DATE: Entered STN: 20011023
Last Updated on STN: 20020420
Entered Medline: 20011219

AB **Citron-kinase** (**Citron**-K) is a Rho effector working in cytokinesis. It is enriched in cleavage furrow, but how Rho mobilizes **Citron**-K remains unknown. Using anti-**Citron** antibody and a **Citron**-K Green Fluorescence Protein (GFP)-fusion, we monitored its localization in cell cycle. We have found: (1) **Citron**-K is present as aggregates in interphase cells, disperses throughout the cytoplasm in prometaphase, translocates to cell cortex in anaphase and accumulates in cleavage furrow in telophase; (2) Rho colocalizes with **Citron**-K in the cortex of ana- to telophase cells and the two proteins are concentrated in the cleavage furrow and to

the midbody; (3) inactivation of Rho by C3 exoenzyme does not affect the dispersion of **Citron**-K in prometaphase, but prevented its transfer to the cell cortex, and **Citron**-K stays in association with the midzone spindles of C3 exoenzyme-treated cells. To clarify further the mechanism of the Rho-mediated transfer and concentration of **Citron**-K in cleavage furrow, we **expressed** active Val14RhoA in interphase cells **expressing** GFP-**Citron**-K. Val14RhoA **expression** transferred **Citron**-K to the ventral cortex of interphase cells, where it formed band-like structures in a complex with Rho. This structure was localized at the same plane as actin stress fibers, and they exclude each other. Disruption of F-actin abolished the band and dispersed the **Citron**-K-Rho-containing patches throughout the cell cortex. Similarly, in dividing cells, a structure composed of Rho and **Citron**-K in cleavage furrow excludes cortical actin cytoskeleton, and disruption of F-actin disperses **Citron**-K throughout the cell cortex. These results suggest that **Citron**-K is a novel type of a passenger protein, which is dispersed to the cytoplasm in prometaphase and associated with midzone spindles by a Rho-independent signal. Rho is then activated, binds to **Citron**-K and translocates it to cell cortex, where the complex is then concentrated in the cleavage furrow by the action of actin cytoskeleton beneath the equator of dividing cells.

L10 ANSWER 23 OF 25 HCAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:348586 HCAPLUS
DOCUMENT NUMBER: 133:87541
TITLE: p21Waf1/Cip1/Sdi1-induced growth arrest is associated with depletion of mitosis-control proteins and leads to abnormal mitosis and endoreduplicaiton in recovering cells
AUTHOR(S): Chang, Bey-Dih; Broude, Eugenia V.; Fang, Jing; Kalinichenko, Tatiana V.; Abdryashitov, Ravil; Poole, Jason C.; Roninson, Igor B.
CORPORATE SOURCE: Department of Molecular Genetics (M/C 669), University of Illinois at Chicago, Chicago, IL, 60607-7170, USA
SOURCE: Oncogene (2000), 19(17), 2165-2170
CODEN: ONCNES; ISSN: 0950-9232
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Induction of a cyclin-dependent **kinase** inhibitor p21Waf1/Cip1/Sdi1 is an integral part of cell growth arrest associated with senescence and damage response. P21 overexpression from an inducible promoter resulted in senescence-like growth arrest in a **human** fibrosarcoma cell line. After release from p21-induced growth arrest, cells reentered the cell cycle but displayed growth retardation, cell death and decreased **clonogenicity**. The failure to form colonies was associated with abnormal mitosis and endoreduplication in the recovering cells and was correlated with the induced level of p21 and the duration of p21 induction. P21 induction was found to inhibit the **expression** of multiple proteins involved in the execution and control of mitosis. P21-induced depletion of the cellular pools of mitosis-control proteins was followed by asynchronous resynthesis of such proteins after release from p21, which explains the observed mitotic abnormalities. Genetic destabilization in cells recovering from p21-induced growth arrest may conceivably play a role in carcinogenesis and tumor progression.
REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 24 OF 25 MEDLINE on STN
ACCESSION NUMBER: 2000275582 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10816250
TITLE: **Citron**, a Rho target that affects contractility during cytokinesis.

AUTHOR: Madaule P; Furuyashiki T; Eda M; Bito H; Ishizaki T; Narumiya S
CORPORATE SOURCE: Department of Pharmacology, Kyoto University Faculty of Medicine, Sakyo-ku, Kyoto 606-8315, Japan.
SOURCE: Microscopy research and technique, (2000 Apr 15) 49 (2) 123-6. Ref: 25
Journal code: 9203012. ISSN: 1059-910X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200007
ENTRY DATE: Entered STN: 20000714
Last Updated on STN: 20000714
Entered Medline: 20000706

AB The small GTPase Rho, which regulates cell shape, is thought to contribute to cytokinesis. Recently, **Citron** was characterized as a Rho target. This large protein contains a Ser/Thr **kinase** domain related to that of ROCK, another Rho effector. Both endogenous **Citron** and **recombinant Citron** localize to the cleavage furrow in dividing cells and to the midbody in post-mitotic cells. Moreover, overexpression of **Citron** deleted from its C-terminal sequence caused abnormal contractions specifically during cytokinesis, resulting in the formation of multinucleated cells. Cell shape, F-actin, intermediate filaments, and microtubules appeared essentially normal in these cells during interphase. Thus, **Citron** is a Rho effector that appears to function during cytokinesis, modulating its contractile process. In brain, however, **Citron** is highly **expressed** in a subset of neurons as a brain-specific isoform that lacks a **kinase** domain, **Citron**-N. This protein accumulates in synapses and associates to the NMDA receptor via interaction with the adaptor protein PSD95, suggesting that the function of **Citron** is specialized in the neurons.

L10 ANSWER 25 OF 25 MEDLINE on STN DUPLICATE 7
ACCESSION NUMBER: 1998334623 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9668072
TITLE: Different regions of Rho determine Rho-selective binding of different classes of Rho target molecules.
AUTHOR: Fujisawa K; Madaule P; Ishizaki T; Watanabe G; Bito H; Saito Y; Hall A; Narumiya S
CORPORATE SOURCE: Department of Pharmacology, Kyoto University Faculty of Medicine, Sakyo-ku, Kyoto 606, Japan.
SOURCE: Journal of biological chemistry, (1998 Jul 24) 273 (30) 18943-9.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199808
ENTRY DATE: Entered STN: 19980828
Last Updated on STN: 20020420
Entered Medline: 19980820

AB Based on their Rho binding motifs several Rho target molecules can be classified into three groups; class I includes the protein **kinase** PKN, rhophilin, and rhotekin, class II includes the protein **kinases**, Rho-associated coiled-coil containing protein **kinases**, ROCK-I and ROCK-II, and class III includes **citron** . Taking advantage of the selectivity in recognition by these targets between Rho and Rac, we examined the regions in Rho required for selective

binding of each class of Rho target molecules. Yeast two-hybrid assays were performed using Rho/Rac chimeras and either rhophilin, ROCK-I, or **citron**. This study showed the existence of at least two distinct regions in Rho (amino acids 23-40 and 75-92) that are critical for the selective binding of these targets. The former was required for binding to **citron**, whereas the latter was necessary for binding to rhophilin. On the other hand, either region showed affinity to ROCK-I. This was further confirmed by ligand overlay assay using both **recombinant** ROCK-I and ROCK-II proteins. Consistently, Rho/Rac chimeras containing either region can induce stress fibers in transfected HeLa cells, and this induction is suppressed by treatment with Y-27632, a specific inhibitor of ROCK **kinases**. These results suggest that the selective binding of different classes of Rho targets to Rho is determined by interaction between distinct Rho-binding motifs of the targets and different regions of Rho.

```
=> d his

     (FILE 'HOME' ENTERED AT 14:51:02 ON 22 NOV 2004)

     FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS,
     LIFESCI' ENTERED AT 14:51:26 ON 22 NOV 2004
L1       1256226 S KINASE?
L2          1508 S CITRON
L3          2404 S RHO(2W)RAC
L4           226 S L1 AND L2
L5            31 S L3 AND L4
L6            12 DUP REM L5 (19 DUPLICATES REMOVED)
L7       6800229 S CLON? OR EXPRESS? OR RECOMBINANT
L8           112 S L4 AND L7
L9            38 S HUMAN AND L8
L10           25 DUP REM L9 (13 DUPLICATES REMOVED)

=> e webster m/au
E1             2      WEBSTER LYNN R/AU
E2            10      WEBSTER LYNNE/AU
E3           830 --> WEBSTER M/AU
E4           183      WEBSTER M A/AU
E5             4      WEBSTER M B/AU
E6             9      WEBSTER M C/AU
E7            51      WEBSTER M D/AU
E8             4      WEBSTER M DOROTHY/AU
E9           145      WEBSTER M E/AU
E10           51      WEBSTER M E D/AU
E11          115      WEBSTER M F/AU
E12            1      WEBSTER M F H/AU

=> s e3
L11          830 "WEBSTER M"/AU

=> e yan c/au
E1             1      YAN BUYU/AU
E2             1      YAN BY ZHANQING/AU
E3          1070 --> YAN C/AU
E4             2      YAN C B/AU
E5           123      YAN C C/AU
E6             6      YAN C C S/AU
E7             3      YAN C CHAN/AU
E8            16      YAN C D/AU
E9             1      YAN C D L/AU
E10           21      YAN C F/AU
E11           48      YAN C G/AU
E12          464      YAN C H/AU
```

```
=> s e3
L12         1070 "YAN C"/AU

=> e difrancesco v/au
E1             1      DIFRANCESCO U/AU
E2             1      DIFRANCESCO U M/AU
E3            99 --> DIFRANCESCO V/AU
E4            17      DIFRANCESCO VALENTINA/AU
E5             1      DIFRANCESCOL/AU
E6             1      DIFRANCESO D/AU
E7             2      DIFRANCESO L/AU
E8             1      DIFRANCESO R/AU
E9             1      DIFRANCESO ROBIN/AU
E10            1      DIFRANCESSO L/AU
E11            6      DIFRANCIA C/AU
E12            4      DIFRANCIA CELENE/AU

=> s e3-e4
L13          116 ("DIFRANCESCO V"/AU OR "DIFRANCESCO VALENTINA"/AU)

=> e beasley e m/au
E1             1      BEASLEY E H/AU
E2             6      BEASLEY E L/AU
E3           314 --> BEASLEY E M/AU
E4             7      BEASLEY E O/AU
E5             1      BEASLEY E S G/AU
E6             2      BEASLEY E T/AU
E7             4      BEASLEY E W/AU
E8             2      BEASLEY E W 3RD/AU
E9             2      BEASLEY E W III/AU
E10            1      BEASLEY E W JR/AU
E11            1      BEASLEY EDWARD E/AU
E12            1      BEASLEY EDWARD EVANS/AU

=> s e3
L14          314 "BEASLEY E M"/AU

=> d his

     (FILE 'HOME' ENTERED AT 14:51:02 ON 22 NOV 2004)

     FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS,
     LIFESCI' ENTERED AT 14:51:26 ON 22 NOV 2004
L1        1256226 S KINASE?
L2           1508 S CITRON
L3           2404 S RHO(2W)RAC
L4            226 S L1 AND L2
L5             31 S L3 AND L4
L6             12 DUP REM L5 (19 DUPLICATES REMOVED)
L7        6800229 S CLON? OR EXPRESS? OR RECOMBINANT
L8            112 S L4 AND L7
L9             38 S HUMAN AND L8
L10            25 DUP REM L9 (13 DUPLICATES REMOVED)
                  E WEBSTER M/AU
L11           830 S E3
                  E YAN C/AU
L12          1070 S E3
                  E DIFRANCESCO V/AU
L13           116 S E3-E4
                  E BEASLEY E M/AU
L14           314 S E3

=> s l11 or l12 or l13 or l14
```

```
L15       2182 L11 OR L12 OR L13 OR L14

=> s l4 and l15
L16          1 L4 AND L15

=> d all

L16  ANSWER 1 OF 1  HCAPLUS  COPYRIGHT 2004 ACS on STN
AN   2003:851250  HCAPLUS
DN   139:346785
ED   Entered STN:  30 Oct 2003
TI   Cloning, sequence and characterization of a human citron
     kinase homolog gene
IN   Wei, Ming-Hui; Chaturvedi, Kabir; DiFrancesco, Valentina;
     Beasley, Ellen M.
PA   Applera Corporation, USA
SO   U.S., 78 pp., Cont.-in-part of U.S. Ser. No. 804,471.
     CODEN: USXXAM
DT   Patent
LA   English
IC   ICM  C12N009-12
     ICS  C12N001-20; C12N005-00; C12N015-00; C07H021-04
NCL  435194000; 435320100; 435325000; 435252300; 435006000; 536023200
CC   3-3 (Biochemical Genetics)
     Section cross-reference(s): 7, 13
FAN.CNT 3
     PATENT NO.           KIND   DATE        APPLICATION NO.          DATE
     ---------------      ----   --------    --------------------     --------
PI   US 6638745            B1    20031028    US 2001-916204           20010727
     US 2002132322         A1    20020919    US 2001-804471           20010313
     US 6479269            B2    20021112
     WO 2003012034         A2    20030213    WO 2002-US23268          20020723
     WO 2003012034         A3    20031016
     WO 2003012034         C2    20040304
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
             PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
             UA, UG, US, UZ, VN, YU, ZA, ZM, ZW
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
             KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
             FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF,
             CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
     EP 1419242            A2    20040519    EP 2002-791541           20020723
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK
     US 2003049795         A1    20030313    US 2002-282048           20021029
     US 6692948            B2    20040217
PRAI US 2001-804471        A2    20010313
     US 2001-916204        A     20010727
     WO 2002-US23268       W     20020723
CLASS
 PATENT NO.        CLASS   PATENT FAMILY CLASSIFICATION CODES
 --------------    -----   ----------------------------------------------
 US 6638745        ICM     C12N009-12
                   ICS     C12N001-20; C12N005-00; C12N015-00; C07H021-04
                   NCL     435194000; 435320100; 435325000; 435252300; 435006000;
                           536023200
 US 6638745        ECLA    C12N009/12B1; C12Q001/48B; C12Q001/68M6B; G01N033/573
 US 2003049795     ECLA    C12N009/12B1; C12Q001/48B; C12Q001/68M6B; G01N033/573
AB   The cDNA and genomic sequences and the encoded amino acid sequence of a
     human kinase that is related to the citron
     kinase subfamily are provided.  Chromosomal mapping of the
```

citron kinase homolog gene, tissue-specific expression profile and structural motifs of the polypeptide are provided. Intron/exon structure and SNPs of the **citron kinase** homolog gene are also identified. The present invention specifically provides isolated peptide and nucleic acid mols., methods of identifying orthologs and paralogs of the **kinase** peptides, and methods of identifying modulators of the **kinase** peptides.

ST **citron kinase** homolog gene sequence human

IT Alleles
DNA sequences
Genetic mapping
Human
Molecular cloning
Plasmid vectors
Protein motifs
Protein sequences
Viral vectors
cDNA sequences
(cloning, sequence and characterization of human **citron kinase** homolog gene)

IT Drug screening
(cloning, sequence and characterization of human **citron kinase** homolog gene in relation to)

IT Genetic element
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(exon, intron/exon structure; cloning, sequence and characterization of human **citron kinase** homolog gene)

IT Animal tissue
(expression profile; cloning, sequence and characterization of human **citron kinase** homolog gene)

IT Gene, animal
RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); USES (Uses)
(for **citron kinase** homolog; cloning, sequence and characterization of human **citron kinase** homolog gene)

IT Chromosome
(human 12, **citron kinase** homolog gene mapping to; cloning, sequence and characterization of human **citron kinase** homolog gene)

IT Genetic element
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(intron, intron/exon structure; cloning, sequence and characterization of human **citron kinase** homolog gene)

IT Genetic polymorphism
(single nucleotide; cloning, sequence and characterization of human **citron kinase** homolog gene)

IT Bacteriophage
(vector; cloning, sequence and characterization of human **citron kinase** homolog gene)

IT 618520-58-4P
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); PREP (Preparation); USES (Uses)
(amino acid sequence; cloning, sequence and characterization of human **citron kinase** homolog gene)

IT 618129-41-2 618520-57-3
RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); USES (Uses)
(nucleotide sequence; cloning, sequence and characterization of human **citron kinase** homolog gene)

IT 212957-16-9P, **Citron kinase**

RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); PREP (Preparation); USES (Uses)
(sequence homolog; cloning, sequence and characterization of human **citron kinase** homolog gene)

IT 618129-96-7 618129-97-8
RL: PRP (Properties)
(unclaimed protein sequence; cloning, sequence and characterization of a human **citron kinase** homolog gene)

RE.CNT 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Maduale; Nature 1998, V394, P491

=> d his

(FILE 'HOME' ENTERED AT 14:51:02 ON 22 NOV 2004)

FILE 'MEDLINE, EMBASE, BIOSIS, BIOTECHDS, SCISEARCH, HCAPLUS, NTIS, LIFESCI' ENTERED AT 14:51:26 ON 22 NOV 2004

```
L1      1256226 S KINASE?
L2         1508 S CITRON
L3         2404 S RHO(2W)RAC
L4          226 S L1 AND L2
L5           31 S L3 AND L4
L6           12 DUP REM L5 (19 DUPLICATES REMOVED)
L7      6800229 S CLON? OR EXPRESS? OR RECOMBINANT
L8          112 S L4 AND L7
L9           38 S HUMAN AND L8
L10          25 DUP REM L9 (13 DUPLICATES REMOVED)
                E WEBSTER M/AU
L11         830 S E3
                E YAN C/AU
L12        1070 S E3
                E DIFRANCESCO V/AU
L13         116 S E3-E4
                E BEASLEY E M/AU
L14         314 S E3
L15        2182 S L11 OR L12 OR L13 OR L14
L16           1 S L4 AND L15
```

	Issue Date	Pages	Document ID	Title
1	20041111	253	US 20040224323 A1	PAK5 screening methods
2	20041021	26	US 20040209297 A1	Novel human kinases and polynucleotides encoding the same
3	20041007	86	US 20040197825 A1	Methods and compositions for treating urological disorders using 44390, 54181, 211, 5687, 884, 1405, 636, 4421, 5410, 30905, 2045, 16405, 18560, 2047, 33751, 52872, 14063, 20739, 32544, 43239, 44373, 51164, 53010, 16852, 1587, 2207, 22245, 2387, 52908, 69112, 14990, 18547, 115, 579, 15985, 15625, 760, 18603, 2395, 2554, 8675, 32720, 4809, 14303, 16816, 17827, 32620, 577, 619, 1423, 2158, 8263, 15402, 16209, 16386, 21165, 30911, 41897, 1643, 2543, 9626, 13231, 32409, 84260, 2882, 8203, 32678, or 55053
4	20041007	190	US 20040197792 A1	Novel Kinases
5	20040513	207	US 20040091993 A1	Isolated human kinase proteins, nucleic acid molecules encoding human kinase proteins, and uses thereof
6	20040422	253	US 20040076955 A1	Methods of diagnosis of bladder cancer, compositions and methods of screening for modulators of bladder cancer
7	20040318	209	US 20040053317 A1	Gene segregation and biological sample classification methods

	Issue Date	Pages	Document ID	Title
8	20040318	243	US 20040053248 A1	Novel nucleic acids and polypeptides
9	20040318	287	US 20040053245 A1	Novel nucleic acids and polypeptides
10	20040304	207	US 20040043926 A1	Novel proteins and nucleic acids encoding same
11	20040226	395	US 20040038223 A1	Novel proteins and nucleic acids encoding same
12	20040129	241	US 20040018189 A1	Nucleic acid and corresponding protein entitled 121P2A3 useful in treatment and detection of cancer
13	20040115	73	US 20040010136 A1	Composition for the detection of signaling pathway gene expression
14	20040115	49	US 20040009502 A1	Identification and tissue distribution of two novel spliced variants of the mouse LATS2 gene
15	20031204	232	US 20030224355 A1	Mutations in the diabetes susceptibility genes hepatocyte nuclear factor (HNF) 1 alpha (alpha), HNF-1beta and HNF-4alpha
16	20031127	103	US 20030220224 A1	Novel polynucleotides encoding the human citron kinase polypeptide, BMSNKC_0020/0021
17	20030501	78	US 20030082511 A1	Identification of modulatory molecules using inducible promoters
18	20030313	222	US 20030050230 A1	STE20-RELATED PROTEIN KINASES

	Issue Date	Pages	Document ID	Title
19	20030313	81	US 20030049795 A1	Isolated human kinase proteins, nucleic acid molecules encoding human kinase proteins, and uses thereof
20	20030313	52	US 20030049695 A1	PDZ domain interactions and lipid rafts
21	20030227	122	US 20030040089 A1	Protein-protein interactions in adipocyte cells
22	20030130	207	US 20030022340 A1	Isolated human kinase proteins, nucleic acid molecules encoding human kinase proteins, and uses thereof
23	20021031	89	US 20020160483 A1	13245, a novel human myotonic dystrophy type protein kinase and uses therefor
24	20020919	184	US 20020132322 A1	ISOLATED HUMAN KINASE PROTEINS, NUCLEIC ACID MOLECULES ENCODING HUMAN KINASE PROTEINS, AND USES THEREOF
25	20020905	26	US 20020123622 A1	Novel human kinases and polynucleotides encoding the same
26	20020801	34	US 20020102553 A1	Molecular markers for the diagnosis of alzheimer's disease
27	20040601	80	US 6743619 B1	Nucleic acids and polypeptides
28	20040511	26	US 6734009 B2	Human kinases and polynucleotides encoding the same
29	20040217	66	US 6692948 B2	Isolated human kinase proteins
30	20040120	202	US 6680188 B2	Isolated human kinase proteins, nucleic acid molecules encoding human kinase proteins, and uses thereof
31	20040120	249	US 6680170 B2	Polynucleotides encoding STE20-related protein kinases and methods of use

	Issue Date	Pages	Document ID	Title
32	20031209	34	US 6660725 B1	Method and composition for modulating amyloidosis
33	20031202	248	US 6656716 B1	Polypeptide fragments of human PAK5 protein kinase
34	20031028	78	US 6638745 B1	Isolated human kinase proteins, nucleic acid molecules encoding human kinase proteins, and uses thereof
35	20030204	34	US 6514686 B2	Method and composition for modulating amyloidosis
36	20021231	65	US 6500938 B1	Composition for the detection of signaling pathway gene expression
37	20021112	202	US 6479269 B2	Isolated human kinase proteins, nucleic acid molecules encoding human kinase proteins, and uses thereof
38	20020716	34	US 6420527 B1	Flavor active modified thaumatin and monellin and methods for their production and use
39	20010213	276	US 6187533 B1	Mutations in the diabetes susceptibility genes hepatocyte nuclear factor (HNF) 1 alpha (.alpha.), HNF1.beta. and HNF4.alpha.
40	20000829	60	US 6111072 A	Rho target protein human mDia and gene encoding same

	Issue Date	Pages	Document ID	Title
1	20041021	26	US 20040209297 A1	Novel human kinases and polynucleotides encoding the same
2	20041007	190	US 20040197792 A1	Novel Kinases
3	20040513	207	US 20040091993 A1	Isolated human kinase proteins, nucleic acid molecules encoding human kinase proteins, and uses thereof
4	20040422	253	US 20040076955 A1	Methods of diagnosis of bladder cancer, compositions and methods of screening for modulators of bladder cancer
5	20040318	209	US 20040053317 A1	Gene segregation and biological sample classification methods
6	20040318	243	US 20040053248 A1	Novel nucleic acids and polypeptides
7	20040318	287	US 20040053245 A1	Novel nucleic acids and polypeptides
8	20040304	207	US 20040043926 A1	Novel proteins and nucleic acids encoding same
9	20040226	395	US 20040038223 A1	Novel proteins and nucleic acids encoding same
10	20040129	241	US 20040018189 A1	Nucleic acid and corresponding protein entitled 121P2A3 useful in treatment and detection of cancer
11	20040115	73	US 20040010136 A1	Composition for the detection of signaling pathway gene expression
12	20040115	49	US 20040009502 A1	Identification and tissue distribution of two novel spliced variants of the mouse LATS2 gene

	Issue Date	Pages	Document ID	Title
13	20031204	232	US 20030224355 A1	Mutations in the diabetes susceptibility genes hepatocyte nuclear factor (HNF) 1 alpha (alpha), HNF-1beta and HNF-4alpha
14	20031127	103	US 20030220224 A1	Novel polynucleotides encoding the human citron kinase polypeptide, BMSNKC_0020/0021
15	20030501	78	US 20030082511 A1	Identification of modulatory molecules using inducible promoters
16	20030313	81	US 20030049795 A1	Isolated human kinase proteins, nucleic acid molecules encoding human kinase proteins, and uses thereof
17	20030227	122	US 20030040089 A1	Protein-protein interactions in adipocyte cells
18	20030130	207	US 20030022340 A1	Isolated human kinase proteins, nucleic acid molecules encoding human kinase proteins, and uses thereof
19	20020919	184	US 20020132322 A1	ISOLATED HUMAN KINASE PROTEINS, NUCLEIC ACID MOLECULES ENCODING HUMAN KINASE PROTEINS, AND USES THEREOF
20	20020905	26	US 20020123622 A1	Novel human kinases and polynucleotides encoding the same
21	20020801	34	US 20020102553 A1	Molecular markers for the diagnosis of alzheimer's disease
22	20040511	26	US 6734009 B2	Human kinases and polynucleotides encoding the same
23	20040217	66	US 6692948 B2	Isolated human kinase proteins

	Issue Date	Pages	Document ID	Title
24	20040120	202	US 6680188 B2	Isolated human kinase proteins, nucleic acid molecules encoding human kinase proteins, and uses thereof
25	20031209	34	US 6660725 B1	Method and composition for modulating amyloidosis
26	20031028	78	US 6638745 B1	Isolated human kinase proteins, nucleic acid molecules encoding human kinase proteins, and uses thereof
27	20030204	34	US 6514686 B2	Method and composition for modulating amyloidosis
28	20021231	65	US 6500938 B1	Composition for the detection of signaling pathway gene expression
29	20021112	202	US 6479269 B2	Isolated human kinase proteins, nucleic acid molecules encoding human kinase proteins, and uses thereof
30	20010213	276	US 6187533 B1	Mutations in the diabetes susceptibility genes hepatocyte nuclear factor (HNF) 1 alpha (.alpha.), HNF1.beta. and HNF4.alpha.

	Issue Date	Pages	Document ID	Title
1	20041111	253	US 20040224323 A1	PAK5 screening methods
2	20040513	207	US 20040091993 A1	Isolated human kinase proteins, nucleic acid molecules encoding human kinase proteins, and uses thereof
3	20040318	209	US 20040053317 A1	Gene segregation and biological sample classification methods
4	20040129	241	US 20040018189 A1	Nucleic acid and corresponding protein entitled 121P2A3 useful in treatment and detection of cancer
5	20040115	49	US 20040009502 A1	Identification and tissue distribution of two novel spliced variants of the mouse LATS2 gene
6	20030313	222	US 20030050230 A1	STE20-RELATED PROTEIN KINASES
7	20030313	81	US 20030049795 A1	Isolated human kinase proteins, nucleic acid molecules encoding human kinase proteins, and uses thereof
8	20030130	207	US 20030022340 A1	Isolated human kinase proteins, nucleic acid molecules encoding human kinase proteins, and uses thereof
9	20020919	184	US 20020132322 A1	ISOLATED HUMAN KINASE PROTEINS, NUCLEIC ACID MOLECULES ENCODING HUMAN KINASE PROTEINS, AND USES THEREOF
10	20040217	66	US 6692948 B2	Isolated human kinase proteins
11	20040120	202	US 6680188 B2	Isolated human kinase proteins, nucleic acid molecules encoding human kinase proteins, and uses thereof

	Issue Date	Pages	Document ID	Title
12	20040120	249	US 6680170 B2	Polynucleotides encoding STE20-related protein kinases and methods of use
13	20031202	248	US 6656716 B1	Polypeptide fragments of human PAK5 protein kinase
14	20031028	78	US 6638745 B1	Isolated human kinase proteins, nucleic acid molecules encoding human kinase proteins, and uses thereof
15	20021112	202	US 6479269 B2	Isolated human kinase proteins, nucleic acid molecules encoding human kinase proteins, and uses thereof

	L #	Hits	Search Text
1	L1	1	"6734009".pn.
2	L2	239827	vetor$2 or host$2
3	L3	377204	vector$2 or host$2
4	L4	1	l1 and l3
5	L5	0	"200040023242".pn.
6	L6	0	"200040023242"
7	L7	1	"20040023242"
8	L8	1	l3 and l7
9	L9	53368	kinase$2
10	L10	446248	human
11	L11	1619	citron
12	L12	17169	l9 same l10
13	L13	40	l11 same l12
14	L14	672338	clon$3 or express$3 or recombuinant
15	L15	30	l13 same l14
16	L16	43708	YAN WEBSTER DIFRANCESCO BEASLEY
17	L17	15	l13 and l16